

INFOBIOMED

NEWSLETTER

N.1 MARCH 2005



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**BIOMEDICAL INFORMATICS
TO SUPPORT INDIVIDUALISED HEALTHCARE**

PORT INDIVIDUALISED HEALTHCARE

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BIOMEDICAL INFORMATICS TO SUPPORT INDIVIDUALISED HEALTHCARE

NEWS

International HapMap Consortium Widens Data Access

<http://www.bio.com/realm/research.jhtml?realm=3&cid=6500168>

The International HapMap Consortium announced that the first draft of the map of human genetic variation, haplotypes is ready six month ahead of schedule, February 2005, and it is a more complete version that first planned.

The project was launched in October 2002 and it was initially set for release on September 2005. The objective of this project "is to compare the genetic sequences of different individuals to identify chromosomal regions where genetic variants are shared".

(<http://www.hapmap.org/thehapmap.html.en>)

The haplotype map, or HapMap, first version consists of 1 million markers of genetic variation, called single nucleotide polymorphisms (SNPs). "The next goal set by the Consortium is to develop a better and improved version five times denser than the original one".

Phase I allowed scientists to carry out an extensive analysis, that will be published along the year 2005, of the human genome that would not have been possible to do with DNA sequences alone. Phase II of the project will use rapid, high-throughput genotyping to build a more complete map by testing another 4.6 million SNPs from publicly available databases, and the addition of that information to the map will allow the discovery of genes in specific regions of the genome in a more precise manner. "This will increase the density of SNP "signposts" across the genome from the current average of one every 3,000 bases to about one every 600 bases".

According to Karen Kennedy (science program manager at the Wellcome Trust) HapMap is already being used to search for genes associated with common diseases as well as genes involved in the responses to the different drugs, and she believes that Phase II will allow to obtain results faster and more efficiently.

Access to the HapMap data can be done through free public databases, such as the HapMap Data Coordination Center (<http://www.hapmap.org>), the NIH-funded National Center for Biotechnology Information's dbSNP

(<http://www.ncbi.nlm.nih.gov/projects/SNP/>)

and the JSNP Database in Japan

(<http://snp.ims.u-tokyo.ac.jp/>).

Sources:

<http://www.nih.gov/news/pr/feb2005/nhgri-07.htm>

<http://www.genome.gov/13014173>

http://bio.com/newsfeatures/newsfeatures_research.jhtml?cid=7800022

Report on the Biomedical Informatics Expert Panel (BIEP): Dr. Peter T. Highnam, Senior Advisor, Office of the Director, NCR

"Dr. Highnam reported that, in January 2004, NCR (Division for Biomedical Technology Research and Research Resources) convened the first meeting of the Biomedical Informatics Expert Panel (BIEP). The BIEP is composed of experts in areas of biomedical research and informatics.

The purpose of the BIEP is to guide NCR staff in developing wide-ranging research tools, including tools required for accessing virtual laboratories, scaleable computing, tools for collaboratories and data sharing, data management tools, and a state-of-the-art bioinformatics toolbox.

The BIEP was formed in direct response to the challenges represented by the increasing complexity of research and the marked increase in the volume of data generated. The informatics infrastructure must be in place to ensure that research progress will not be hampered.

In addition to extensive discussions, the Panel heard presentations in three areas.

The Biomedical Informatics Research Network (BIRN) was described in depth, and future plans were covered by Dr. Mark Ellisman (University of California at San Diego), Dr. Greg McCarthy (Duke University), and Dr. Michael Marron (NCR). The NCR strategic investments to increase the computer network connectivity into and within six northwestern IDeA states in the NCR Biomedical

Research Infrastructure Network (BRIN) program were covered by Dr. Gwen Jacobs (Montana State), Dr. Ron Johnson (University of Washington), and Dr. Sidney McNairy (NCCR). A discussion on current NCCR plans to provide substantial improvements in informatics infrastructure to support clinical research was summarized by Dr. Elaine Collier (NCCR) and Dr. Peter Highnam (NCCR)".

Sources:

<http://www.ncrr.nih.gov/newspub/minjan04.asp>

Karolinska Institutet and Affymetrix Announce Translational Medicine Strategic Alliance



**KAROLINSKA
INSTITUTET**
a medical university



"Affymetrix Inc., California, USA and Karolinska Institutet, in Stockholm, Sweden, announced that they have entered into a strategic alliance designed to improve healthcare by accelerating the translation of basic genetic research into tools for better diagnosis, prognosis, and treatment".

The plan is to collaborate during the next five years in projects of diseases that affect large number of people worldwide such as atherosclerosis, breast cancer asthma, rheumatoid arthritis and dyslexia with the aim of improving and developing clinical methods and drugs to treat these diseases and therefore improving quality of life of the people suffering from the diseases.

They will perform genetic analyses and measurements of gene expression with the aim of establishing true clinical relevance in key areas of unmet medical needs for this, they will use sufficiently large sample sizes of the population to be studied.

Both the dean of research at Karolinska Institutet, Professor Jan Carlstedt-Duke and the European Site Manager and Vice President, Affymetrix, Patrick Kelly made comments highlighting the importance of this cooperation to increase the understanding of genetic factors in disease emergence and in the prediction of disease susceptibility and individual's response to drugs that will move the translational medicine field forward leading towards better personalised medicine and health.

Sources:

http://www.bio.com/industryanalysis/industry-analysis_news.jhtml?cid=7800040

http://www.info.ki.se/article_en.html?ID=3063

The transition from LocusLink to Entrez Gene



The NCBI has carried out the transition from LocusLink to Entrez Gene. This new resource is more tightly linked with other databases via the Entrez interface since it is an Entrez database itself. It provides a "unified environment for genes defined by sequence and/or in NCBI's Map Viewer".

Currently, it has information on hundreds of organisms with more than 1.3 million records. The 1st of March this year the change was completed, and no more updates to LocusLink or its products will be done and the web interface will be retired although entries to LocusLink are automatically redirected to Entrez Gene.

<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene>

Source: *biolInform* v9, n4; January 31st, 2005

BioPax Standards Initiatives

BioPax is one of the projects of the Memorial Sloan Kettering Cancer Center's (MSKCC) Computational Biology Center (<http://www.cbio.mskcc.org/>) supporting cancer research.

The aim of BioPax is to create an XML-based standard for exchanging various types of biological pathway data that will also facilitate the sharing of pathways information between existing databases, both public and private.

The project began at the 4th BioPathways Consortium Meeting (ISMB'02 Conference). The first phase of the project, called level 1, was released November 19th, 2004 and provided an exchange language for sharing metabolic pathway data. The second phase, level 2, actually on the way, will support molecular interaction databases such as BIND and DIP. An initial draft is provided to generate discussion and feedback from the community, which will be the base for future changes to be made before the next version of level 2 is released.

The collaboration with the HUPO's and European Bioinformatics Institute's Protein Standards Initiative

(<http://psidev.sourceforge.net/mi/xml/doc/user/> and

<http://www.ebi.ac.uk/Information/meetings/psi.html>)

will ensure that BioPax Level 2 is compatible the PSI's own standard for molecular interaction data (PSI-MI). Level 3 is planned to cover signal transduction and regulatory networks.

Future levels will go into abstract relationships between biological entities, cell-level interactions, and conclusions from binding assays (annotated with statistical confidence measures).

BioPax only covers pathway data and therefore it is complementary to the Systems Biology Markup Language, which aims to provide a means of sharing and exchanging the computational models that would use the pathway data.

<http://www.biopax.org/index.html>

Source: *biolinform* v9, n5; February 7, 2005

IEEE promotes Bioinformatics Standards

IEEE Standards Association

PROJECT SEARCH IEEE-SA MEMBER AREA

The Institute of Electrical and Electronics Engineers has recently kicked off an effort to formalize several grassroots standards projects in the Bioinformatics community called P1953 and titled 'Bioinformatics Data Structures - Framework and Overview', with the aim of providing a consistent reference system or database framework for maintaining and representing dynamic biological information.

The scope of this project as described in the web page of the IEEE

(<http://standards.ieee.org/cgibin/status>) "is to develop a framework for standards and protocols, incorporating existing standards where appropriate, to support the bioinformatics sciences with common definition, storage and exchange of information between them.

The project will define efforts in the area of nomenclature, databases, access protocols, benchmarks, and validation suites for a variety of bioinformatics data (e.g., genomics, proteomics, transcriptomes, gene ontology, structural ontology, biological pathways, pharmacogenomics and more)". The first phase of this project will probably be the Sequence Ontology (SO) as according to *bio1NFORM* January 10th magazine (v 9,n 1). This project has gained support from the bioinformatics community because of its association with Gene Ontology (GO).

It is believed that due to its smaller size it will be easier to reach a large consensus.

With the Standard references system in Bioinformatics, the IEEE aims to provide very clear guidelines for assuring the flexibility of standards, an important consideration since ontologies evolve they are not static, while, at the same time, providing, as it says in its web page, "a consistent reference system or database framework (a stable core) for maintaining and representing dynamic biological information".

This organization requires the collaboration of several collectives to develop such ontology and to gain the approval of users, producers and other interested parties, since the "purpose is to provide

a framework standard for the development of new standards where needed, incorporating existing standards where appropriate and providing a consistent interface for the development of common solutions for discovery, collection, access, and use of bioinformatics data". So, this initiative seeks to formalize existing standards, rather than develop new ones from scratch.

<http://grouper.ieee.org/groups/1953/index.html>
<http://www.csbcon.org/>
<http://standards.ieee.org/board/nes/projects/1953.pdf>

Source: *bioInform* v9 n1. January 10, 2005

National Centers for Biomedical Computing

The United States of America has just approved the creation of four new national centers, called National Centers for Biomedical Computing, to develop an international computing framework in biomedical computation.

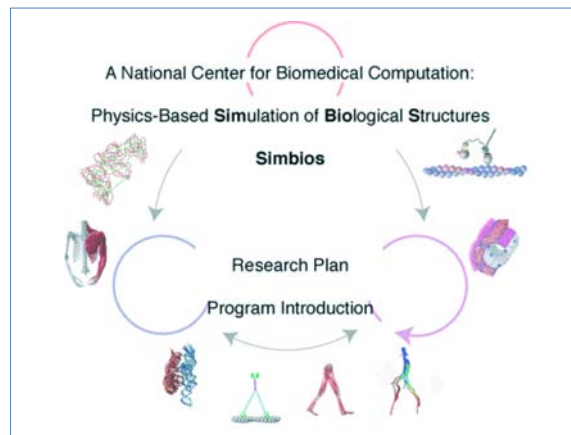
These centers' main goal is to create the core of a computing infrastructure to speed progress in biomedical research. New software programs and other tools will be developed to enable the research community to analyse, model, simulate and share data of human diseases.

The centers are part of the National Institutes of Health RoadMap for Medical Research.

Researchers related to the four centers will create new computational tools by means of data collected in both the lab and the clinic. A main goal of the centers is to distribute the developed tools and to train future users.

Research teams of the four new centers consist of researchers in computation, biology and behavioral science to collaborate in several projects including:

Physics-Based Simulation of Biological Structures Center, where new tools for biological systems simulation will be created (Stanford, <http://cbmc-web.stanford.edu/simbios/>).



National Alliance for Medical Image Computing will develop software to integrate analysis and visualise data from a variety of sources to better understand a broad range of diseases (Brigham and Women's Hospital, <http://www.na-mic.org/>).



Center for Computational Biology will construct "computational atlases", sets of maps featuring different biological data, using as platforms for the biological processes and human diseases study. These atlases collect computational and mathematical approaches to study genes, cells, systems and the whole brain (UCLA, <http://www.ioni.ucla.edu/CCB/>).

Informatics for Integrating Biology and the Bedside Center will develop computational tools for clinical researchers to obtain the gain of the genomic for better understanding of diseases as common as diabetes or high blood pressure (Brigham and Women's Hospital, <http://www.partners.org/i2b2>)

The creation of the four centers is the first step in the National Institutes of Health Roadmap plan for bioinformatics and computational biology.

Sources:

<http://www.nigms.nih.gov/news/ncbc.html>
<http://www.bisti.nih.gov/ncbc/index.cfm>

INFOBIOMED PROFILES

MI-EMC



Medical Informatics is an interdisciplinary research group within the Erasmus MC, University Medical Center Rotterdam. The group studies new methods for acquiring, representing, processing, and managing knowledge and data within health care and the biomedical sciences.

Our research clusters around two main themes: structuring medical data, with the electronic patient record as an important application area, and structuring medical knowledge, with decision support as main focus.

In our research line structuring medical data we concentrate on the nature and structure of medical data. Ideally, medical data recorded in the context of clinical care should not only be available for patient care, but also be accessible for other purposes, such as scientific research, quality assurance, or management. Scientific research, however, has shown that the purpose of data collection is closely related to the nature and content of the data recorded. Different usage of the data creates different demands: data requirements in the context of a clinical trial are different than those in the context of management or quality assurance.

Our research is focused on generic models that are applicable to different specialties. The models, however, have to be usable in daily practice. An essential part of this research, therefore, is the validation of these models in daily care. Once electronic patient records are available, our research focus shifts to the actual use of the data for multiple purposes. In close collaboration with clinicians, we study systems aimed at improving the quality of care.

Together with other disciplines we also analyze observational databases and study issues involved in naturalistic trials. Not only do we address clinical questions, we also experiment with methodological innovations that are focused on combining retrospective and prospective designs in a single environment.

In our research line structuring medical knowledge we investigate the formalization of medical knowledge; that is, the description of knowledge according to a formal representation so that the knowledge can be made operational in a computer system. We do not limit ourselves to knowledge that is provided by experts or is described in journals or books, but also focus on the (semi)automatic extraction of knowledge from documented databases. With respect to documented databases, attention is paid to automated learning techniques for modeling medical knowledge, tailored to the specific problems in the medical domain. This includes research in the representation and use of uncertainty in medical knowledge.

It is of utmost importance to test the results of our research (both methodology and prototypes of systems) in the diverse application domains for their usability, in close collaboration with other investigators and clinical partners.

Under this research theme, two application domains in the past years have attracted our special attention.

First, together with the Department of Radiology of the Erasmus MC and in collaboration with the Technical University of Delft, we started a research group in image processing and computer-aided image interpretation.

Second, the recent developments in bioinformatics (that is, the discipline that focuses on the collection, storage, analysis, interpretation, and access of molecular-biological information with the use of information-processing systems) prompted us to initiate complementary research from the perspective of Medical Informatics: extracting information from literature and annotated biomolecular data sets ('text-based searching') and supporting the interpretation of data ('data mining').

IEETA



ieeta instituto de engenharia electronica
e telematica de aveiro

<http://www.ieeta.pt>

The Instituto de Engenharia Electrónica e Telemática de Aveiro (IEETA) is one of the 17 Research Units that belong to the University of Aveiro, with the specific purpose of performing multidisciplinary research and development unit in the fields of Electronics and Telematics, integrated in the international scientific research community and actively contributing for the national social and technological advancement.

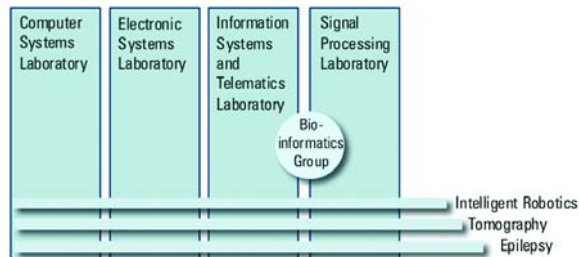
IEETA was involved in the past in several EU projects in the area of health. It was recently the coordinator of IST-11567 (TEAM-HOS) and IST-2001-39013 (INFOGENMED).

Besides EU funded projects IEETA is also leading several research and development projects and technology transfer projects funded by the Portuguese Agency of Research.

The group has a strong expertise in biomedical engineering and medical informatics with collaborations with national and international research and clinical groups.

The Institute has currently a staff of 72 persons of which 48 are PhDs, developing their activities in four laboratories and three transverse activities, nurturing strong links with other Research Units of the University.

It has the following organization:



Focusing specifically in the Bioinformatics Group, it joins several researchers with expertise in areas such as molecular biology, chemistry, statistics, computing and information systems.

Current research lines include:

- Computer methods for genome data analysis;
- Research on data management in proteomics;
- Advanced signal processing techniques and tools for Bioinformatics;
- Integration of genetic and clinical information sources;
- Integration of clinical and genetic data in the Electronic Health Record;
- Integration of clinical information (images, signals) and visualization;
- Bridging bio and medical informatics (signal processing, image analysis...);
- Distributed environments in healthcare.

Other areas that are currently developed at IEETA with interest for the network are:

- Image and signal processing;
- Digital libraries applied to health.

RESOURCES

New Comparative Toxicogenomics Database



CTD: <http://ctd.mdibl.org>
<http://www.bio.com/realm/research.jhtml?realmId=3&cid=7100044>

The Mount Desert Island Biological Laboratory has publicly released a prototype of the Comparative Toxicogenomics Database (CTD: <http://ctd.mdibl.org>).

This database “identifies interactions between chemicals and genes in diverse organisms to advance understanding of how environmental chemicals affect human health”. It provides centralized, integrated and curated molecular and toxicology data from diverse organisms, both vertebrates and invertebrates. It integrates data such as gene sequences, chemicals, references, taxonomic and Gene Ontology data with the purpose of identifying gene-chemical interactions.

The database also “curates “Gene Sets” to place sequences in a comparative context by grouping all sequences from diverse species for a gene or related genes”. The data obtained from this comparative context might provide new insight into the differences in the response to chemicals between organisms based on their gene structure, something impossible up to now.

CTD prototype is a community-supported public resource funded by the National Institute of Environmental Health Sciences, one of the National Institutes of Health. It is still being developed. To improve it, scientists are encouraged to help in its development by sending in feedback and submitting data sets via the website (ctd@mdibl.org).

Sources: <http://bio.com> on the 01/11/05 and the CTD web page

MyNCBI



This resource substitutes PubMed© Cubby as PubMed's bibliographic tool.

It stores the searches made just like cubby and includes new functionalities that facilitate the handling of the stored searches. My NCBI requires user to register but registered Cubby users do not have to register again.

The stored searches can be programmed to be automatically updated and to send the updates to a given e-mail address.

It is not necessary to make a new PubMed search on later dates to find out any new bibliographic references.

To read more about this resource:
http://www.nlm.nih.gov/pubs/techbull/jf05/jf05_myncbi.html

PANTHER



Applied Biosystems has released its classification system Protein Through Evolutionary Relationships (PANTHER). They plan to integrate PANTHER with the database InterPro and make it consistent with the database PIRSF in the near future.

PANTHER classifies proteins (and their corresponding genes) with the goal of facilitating their subsequent analysis. They are classified according to families and subfamilies, molecular functions, biological processes and metabolic pathways.

To carry out the process PANTHER consists of large number of proteins divided in families. These in turn are organized in subfamilies according to their molecular function. The division in subfamilies permits a more accurate correspondence between protein and function. However it is possible to classify new proteins through Hidden Markov Models (HMM) created for each family and subfamily.

The last version of PANTHER (Version 5.0) released Jan 1, 2005 cover about 90% of the proteins coded by mammalian genes, thanks to the 6683 and 31705 catalogued families and subfamilies respectively.

It also includes a number of facilities with respect to the former versions that include: metabolic pathway representation, and its association with families and subfamilies, a methodology to define families and subfamilies and the construction of HMM and parameters to assess sequences with respect to the HMM included in the system.

Source: <https://panther.appliedbiosystems.com/>

EVENTS

Symposium "Pharmacogenomics and Pharmacogenetics: Current Challenges and Bioinformatics Support".

11th and 12th of July 2005. Barcelona, Spain. Anybody interested in participating in this Symposium please contact grib@imim.es.

<http://nemo.imim.es/grib/secciones/research/workshop.htm>

IEEE Computational Systems Bioinformatics Conference.

8-11 August 2005. Stanford, California, USA.

<http://conferences.computer.org/bioinformatics>

AMIA 2005 Annual Symposium. Biomedical and Health informatics: From Foundations to Applications to Policy.

22-26 October. Washington D.C. USA

<http://www.amia.org/meetings/annual/current>

9th Annual International Conference on Research in Computational Molecular Biology (RECOMB2005).

14-18 Mayo. Cambridge, Massachusetts, USA.

<http://www.broad.mit.edu/recomb2005>

2nd. International meeting on the Genetics of Complex Diseases and Isolated Populations.

May 28 to May 31, 2005. Paestum (Amalfi Coast), Italy.

<http://www.geneticisolates.com>

The First INFOBIOMED Training Challenge will take place in Viladrau (Barcelona, Spain) from the 12th to the 16th of September 2005.

The First INFOBIOMED Training Challenge will consist on 2 groups of 5 students with different backgrounds that will work together in a case study that can clearly benefit from an integrative approach. Pharmainformatics has been chosen as the subject of this first edition, and the students will be tutored by the scientist involved in this pilot. The student expenses will be covered and the application deadline is 30th of June 2005. More details can be found in the pdf brochure in our webpage (www.infobiomed.org).

EVENTS

ISBMDA
(International Symposium on Biological and Medical Data Analysis)
November, 10-11, in Aveiro, Portugal.



ISBMDA (International Symposium on Biological and Medical Data Analysis) is an annual conference, realized since 2000, that aims to integrate interdisciplinary research from scientific fields such as statistics, bioinformatics, biomedical informatics and knowledge discovery for biomedical data analysis.

This year, with the endorsement of INFOBIOMED, the **6th edition of ISBMDA** (former ISMDA) will be held in November, 10-11, in Aveiro, Portugal.

Submission of papers is welcome, before June 10, on all aspects of biological and medical data analysis and prediction, namely on the following areas:

- Bioinformatics
- Biomedical informatics
- Medical databases and information systems
- Ontologies and formal representation systems
- Methods and systems for database integration
- Grid-based approaches for data processing
- Data visualization
- Data analysis for image processing
- Information retrieval
- Text and web mining
- Knowledge discovery and data mining
- Statistical methods and tools for biomedical data analysis
- Time series analysis
- Decision support systems

Further information on:
<http://www.ieeta.pt/isbmda05/>

COMMENT

What is Biomedical Informatics?

By Fernando Martin-Sanchez, Isabel Hermosilla G. and F^o Javier V. Martín

When suggesting a definition for Biomedical Informatics (BMI), we could go back to the one in the White Paper developed in the context of BIOINFOMED: “BMI is the emerging technology that aims to put together the worlds of Bioinformatics (BI) and Medical Informatics (MI) in order to facilitate the discovery and creation of novel diagnostic and therapeutic methods in the context of genomic medicine.”

However, a comprehensive definition of BMI should also include diverse aspects that clearly appear in relation with the role of informatics in the new scenario of genomic based medicine:

- Disease is a continuous process and genetic and molecular data should not be treated independently from data concerning the clinical manifestation and clinical progression of the patients.
- Relevant information about a disease goes through several levels related to the levels of organization in the human body (molecules, cells, tissues, organs, body, population.).
- BMI facilitates translational research allowing the “translation” of the discoveries coming from basic research into valid solutions for the clinical environment.
- BMI represents a possible “conducting thread” that allows to interpret the connections between genotype and phenotype and the environmental factors that influence in this relation.

In the last years we have noticed how several names, often used in an interchangeable manner, have been used to name approaches to BMI. Terms such as clinical bioinformatics, clinical genomics and others often appear in literature and in the description of research projects. This short comment will use a figure to try to explain the meaning of these different terms and how BMI relates to each.

If we take into account two different criteria such as the type of data used, and the setting in which the techniques are applied we could see that:

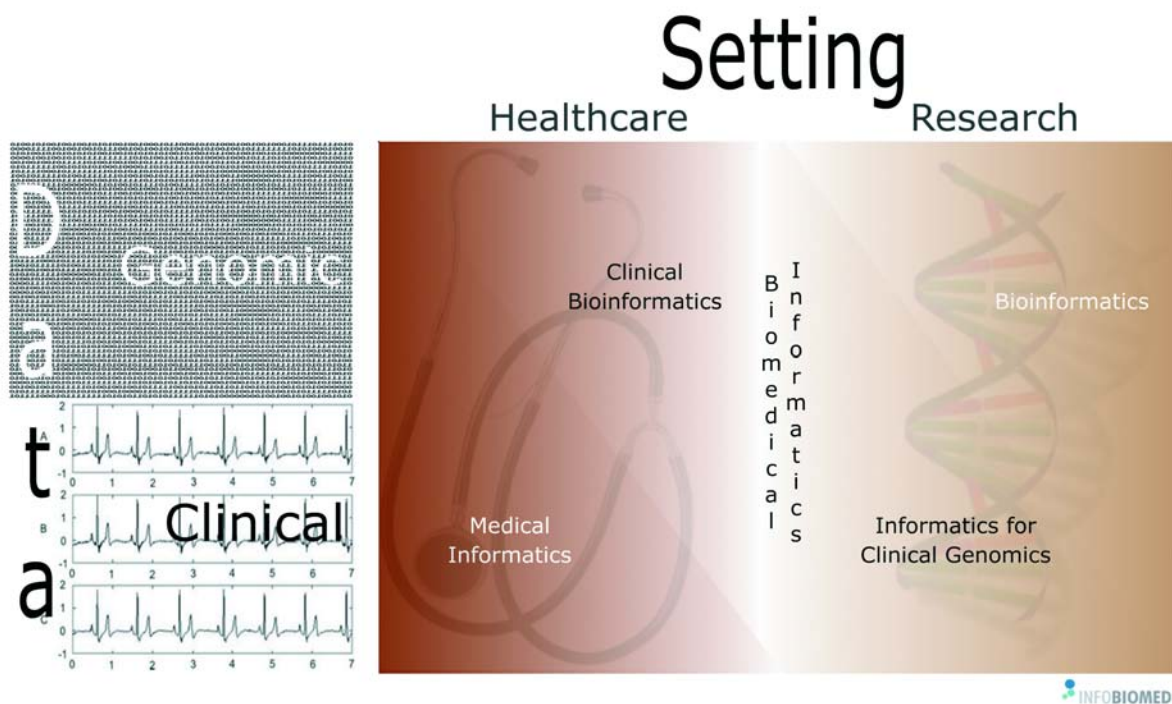
Bioinformatics facilitates processing of genomic and proteomic data in a basic research oriented setting. Medical Informatics uses clinical data in a clinical and healthcare setting. The objective of Clinical Bioinformatics is to facilitate the introduction of genomic and proteomic data of the patients for its use in clinical practice (individualised medicine) while Informatics for Clinical Genomics tries to provide actual clinical data for genomic and proteomic research for the improvement of annotation and validation of the results and to get information about molecular causes of diseases (molecular medicine).

Examples of the last two areas mentioned would be:

- Clinical Bioinformatics:
The works of the HL7 group to model and structure patient genetic data in order to include it in the working model of the digital clinical record.

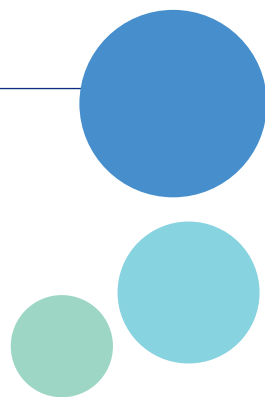
- Informatics for clinical genomics:
Retrieval of clinical data of patients with certain types of tumors from the hospital, anonymization of the information and integration with data from the molecular analysis of these tumors obtained by microarray techniques in which the profiles of differential genetic expression are identified.

We can conclude that BMI includes diverse aspects to facilitate the integration and combined analysis of all the data that are relevant for the study, prevention, diagnosis and treatment of complex diseases, providing tools that make possible an individualised medicine for each patient depending on the phenotypic signs and the genetic load and based in the profound knowledge of the molecular mechanisms that unchain diseases.



Graphic definition of BMI

BIOMEDICAL INFORMATICS
TO SUPPORT INDIVIDUALISED HEALTHCARE



BIOMEDICAL INFORMATICS TO SUPP

<http://www.infobiomed.org>

