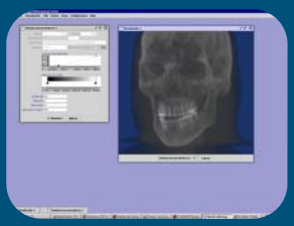
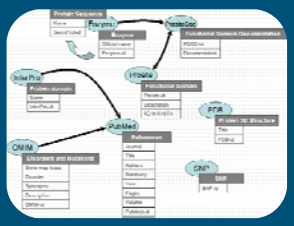
# Biomedical Informatics Group (GIB)

## Universidad Politecnica de Madrid



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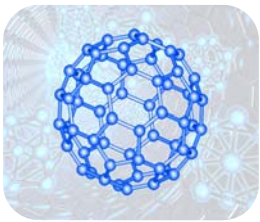
## Nanoinformatics



Some nanoinformatics challenges are, for instance, information management and search, creation of taxonomies and classifications for nanomaterials, the construction of nanomaterials databases, infrastructures for R&D in nanotechnology, or new models and simulations of nanoparticles, among others. We have reported the first reviews of the field and carried out research on various areas: (i) development of an inventory of nano resources, (ii) text mining-based research to extract information of nanoparticles from the scientific literature, (iii) a nanotoxicity searcher, (iv) creation and definition of the area "Translational Nanoinformatics", and (v) a new scientific approach to build visual, "morphospatial" taxonomies of nanoparticles. We led ACTION-Grid, the first EC project on nanoinformatics.

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Mark D Hoover, Nathan A Baker, Frederick Klaessig, Stacey Harper, Juli Klemm and Victor Maojo. Nanoinformatics: Principles and Practice. Elsevier 2014 (in preparation)


## Biomedical Ontologies and Vocabularies

We have used computational ontologies in topics such as ontology-based data integration, query homogenization, data cleaning and mining, clinical-genomic trials, information extraction and retrieval, text mining, building biomedical vocabulary servers, nanoinformatics research, or developing cancer ontologies. We have also introduced a fundamental challenge, proposing a new approach for building "morphospatial" and visual taxonomies of shapes, representing the kind of graphical, "visual" information that is inherent to the shapes of entities such as molecules, organs, nanoparticles, viruses, etc.

In 1997 the GIB decided to build a system —the first in the world— to access Pubmed using MeSH terms in Spanish. Once the terms are specified in Spanish they are automatically translated to English and the query is submitted via Web to the NLM server.

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Rodriguez J, Maojo V, Crespo J, Fernandez I. A concept model for the automatic maintenance of controlled medical vocabularies. Proceedings of Medinfo 1998


## Text Mining & Information Retrieval

Over the last decade, the GIB has been involved in a large number of text mining and information extraction/retrieval projects. We have been particularly active in accessing and extracting knowledge from various unstructured sources, and particularly from the biomedical literature — available in Pubmed. Bringing together structured and text-based sources is an exciting challenge for biomedical informaticians, since most relevant biomedical sources belong to one of these categories. Unfortunately, the methods and tools provided by state-of-the-art database integration tools cannot be reused to bridge together structured and non-structured (text-based) sources, since all of them require the individual sources to be equipped with a logical schema.

To address this issue, we created various approaches based on text mining techniques to automatically create a logical schema for non-structured sources. As seen in other sections, we have widely used text mining techniques in a large number of areas.

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## Bioinformatics and the "Resourceome"

We created the BioInformatics Resource Inventory (BIRI) for automatically discovering and indexing available public bioinformatics, later expanded to medical and nano resources using information extracted from the scientific literature. We also worked on the identification and extraction of DNA sequences and automated database population. Data reported in the biomedical literature are an aid for primer and probe design for microorganism identification, genotyping and gene expression studies. Unfortunately, there are only a few online databases established as repositories for empirically validated primer and probe sequences. Thus, we created an original method for automatically detecting and extracting infectious disease-related primer and probe sequences from scientific papers, applied to all the PubMed Central repository. The data extracted from the manuscripts were then fed into the PubDNA finder database, the first public online resource linking scientific papers to sequences of nucleic acids.

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## Data Mining

In 1995 we carried out a performance comparative analysis between traditional rule-induction algorithms and clustering-based constructive rule induction algorithms. As a benchmark, a database of rheumatoid arthritis (RA) from the Hospital 12 de Octubre was used. A set of clinical prediction rules for prognosis in RA was obtained by applying the most successful methods, selected according to the study outcomes. A panel of medical specialists in RA chose 21 predictive variables and the outcomes. By comparing artificial neural networks, induction and clustering techniques, we were available to extract clinical prediction rules that were successfully tested in clinical practice.

Later we have used data mining techniques for extracting information from heterogeneous databases, using a federated approach. Members of the GIB were also involved in various data mining projects, chairing various data mining international conferences.

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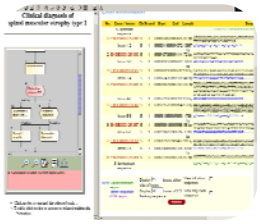
## Clinical Guidelines & Protocols



In 1996, we developed an original specification language to graphically represent guidelines as flowcharts, linked to multimedia information, to facilitate distribution over the Web. This tool was acknowledged by SUN Microsystems as one of the first Java-based tools ever reported in the medical domain. In collaboration with other faculty members at the UPM, we designed a computerized approach to detect inconsistencies in medical knowledge bases. Appropriateness criteria were automatically translated into rules containing propositional variables. This rule set was then checked for inconsistencies. Finally, the set of medical appropriateness criteria was represented in the flowchart format, remotely accessed over the Internet. The GIB developed in 1996-7 a clinical hypertension database for the Hospital Principe de Asturias in Alcala and, in collaboration with the transplant unit at the Hospital Clinico San Carlos in Madrid, we produced a pioneering database and support system for transplantation - one of the first ones in Spain. This database was later used in other Madrid-area hospitals.

**References:**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## Cognitive Science and NBIC


Victor Maojo has taught the course entitled "Cognitive Science" since 1995. Since 2005, the GIB has placed special emphasis on the integration of Cognitive Science within the NBIC Converging Technologies (Nanotechnology-Biology-Information Technologies- Cognitive Science), a challenging multidisciplinary effort launched with support from the US National Science Foundation, later adopted in Europe. Besides our deep involvement in the area of nanotechnology, past research was related to brain patterns of cognitive activity, electroencephalograms (EEGs) and event-related potentials (ERPs). These signals were analyzed and evaluated after patients received and processed lexical information. We analysed maps of brain activity, searching for correlations with psychological parameters and features related to measures of intelligence, extraversion, anxiety or decision making. In addition, we have also analysed the impact of virtual reality in education from a cognitive perspective, later one of the focal points of the NBIC area.

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## Personalized Medicine


The GIB pioneered work linking genomic and clinical information. Advances based on the Human Genome Project have led to personalized medicine opportunities, and with the development of high-throughput techniques for generating genomic profiles of patients this has already led to personalized diagnoses, therapies and drugs, revolutionizing therapeutic procedures and health care. We participate in the EC project P-medicine which has brought together leading research groups in Europe to design and implement technological solutions. Its goals involve sharing large-scale datasets in a secure fashion, performing Virtual Physiological Human simulations and running complex data workflows involving statistical analysis and data mining. Several test-scenarios evaluate clinical trials on cancer —Wilms tumor, breast cancer and leukaemia trials. Personalized medicine and nanomedicine will be one of the fundamental challenges for the next decades, a topic on which GIB has pioneered informatics research.

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## Defining Biomedical Informatics

Since 1998, we aimed to define the field of biomedical informatics, arising from the confluence of bioinformatics and medical informatics. We have carried out a comprehensive review of their potential interactions which led to several integration projects. The GIB participated in the BIOINFOMED study and the INFOBIOMED network of excellence, two EC projects which contributed to define the field. For instance, BIOINFOMED was the first proposal laying a foundation for the Virtual Physiological Human programme of the European Commission. This programme was later funded at the level of 200M€. Recently, we have been partners of the INBIOMEDVision project, which aims to become a consolidated Biomedical Informatics Observatory, especially focused on Europe. A group of scientific leaders in this area, from Europe and the USA, participates in this long-term, broad initiative.

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## Database Integration and Semantic Interoperability


In 2001 the GIB launched INFOGENMED, the first project funded by the EC in the area of clinico-genomic integration. At the GIB, we developed the "ONTOFUSION" system. This provided unified access to multiple, heterogeneous biological and medical data sources from over 1500 public databases. We used the system to integrate significant examples such as OMIM, PubMed, Enzyme, Prosite and Prosite documentation, PDB, SNP, or InterPro. Since then, OntoFusion has become one of the main references in the field. Technological aspects included mapping clinical and genetic concepts and the development of new methods and tools for database integration based on biomedical ontologies, agents and Web services. Subsequently, we developed many semantic-based methods and tools for addressing heterogeneity in biomedical information and the Web. This work has been realized through application of semantic web technologies like RDF, OWL, OWL2, RDQL, SPARQL using ontology alignment and data curation.

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## Big Data and Opinion Mining

The objective of our EC-funded DICODE project is to facilitate and augment collaboration and decision making support in data-intensive and cognitively-complex disparate research disciplines. The DICODE project aims to develop innovative big data methodologies by providing seamless integration and interoperability among existing and new applications under a unique web-based platform. This platform will enable users to work collaboratively, sharing applications and data, to facilitate the decision making tasks. The DICODE approach and platform have been evaluated by experts in three different domains: bioinformatics, medical informatics and social media, with the participation of various leading companies in this area. Text and opinion mining techniques were applied to analyze 'big data' coming from specialized literature and the unstructured Web 2.0. Information in the social networks can facilitate access to population trends and attitudes, which must be analyzed and filtered using cutting-edge techniques and approaches.

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## AFRICA BUILD

For many years, foundations and non-governmental organizations have focused their efforts in Africa by donating cash, electronic devices, or even whole labs. However, a fundamental gap for creating a solid scientific infrastructure is the lack of trained staff and academic professionals. In this context, we coordinate the AFRICA BUILD project to build the infrastructures needed to increase learning, research and collaborative health activities in Africa. We have created the first social network for African biomedical researchers through the AFRICA BUILD Portal —a "facebook for medical professionals in Africa". This facility includes many free and open technological and educational resources for training and support of African students and professionals. Two pilot projects related to training in HIV-AIDS and reproductive health were designed as a proof of the AFRICA BUILD concept. With such an approach, we are building a network of virtual communities in various biomedical topics, fostering new collaborative South-South biomedical initiatives.

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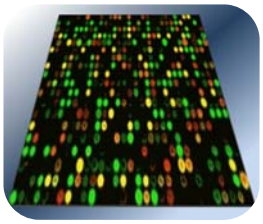
## Clinical Trials and Cancer Research



Since 2004, we have been working on developing models and tools to integrate clinical trials databases, following semantic approaches. Years after working on ACGT (advanced clinic-genomic trials on cancer), the objective of our FP7 INTEGRATE and EURECA projects is to advance research in oncology through a unique accessible biomedical infrastructure integrating diverse datasets, building predictive bionetworks and offering advanced tools to guide diagnosis and therapeutics. Based on multi-centric clinical trials programmes on breast cancer and other oncology domains, INTEGRATE and EURECA exploit a collaborative environment to combine multi-scale biomarkers (from genetic level to tissue level including imaging biomarkers) to define a methodology to improve the prognostic power of practices for assessing modern therapies in cancer treatment. Working together with partners such as Philips and various leading oncology centers from Europe, we aim to develop a new framework for future clinical trials.

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## Image Analysis and Processing

Applications of digital imaging include the enhancement and filtering of noisy images, the segmentation of regions of interest, the extraction of measurements, and shape processing. The main areas of our work have been the following:

(a) Theoretical and practical aspects of morphological connected filtering (which can preserve the shapes and forms in input images), including the so-called "levelings".

(b) Shape interpolation methods that allow to impose shape inclusion restrictions that can preserve, if desired, certain homotopy properties of the interpolated images.

(c) Segmentation techniques, such as variants of the morphological watershed that include shape constraints, and region merging methods. Some application domains have been the segmentation of internal structures of the brain and the extraction of particles in pathology.

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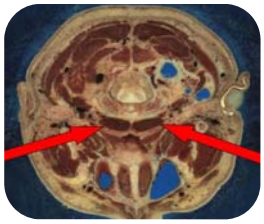
## Biomedical Applications in Imaging



Doctors need tools to use and to manage volumetric radiological data (three-dimensional imaging data, such as TC and MRI). We have worked on applications of 3D visualization of radiological data to navigate inner parts of the body and to model inner structures (using image segmentation techniques as well). We aimed to utilize relatively inexpensive equipment, such as PCs with specialized volumetric visualization hardware, for surgical planning purposes in virtual endoscopies.

We have also worked on medical imaging databases and PACS that are scalable and that can be used in both department-wide applications and in isolated workstation settings. Such applications benefit from an easy-to-use medical image explorer to interact with image databases, allowing, if desired, remote collaboration sessions among doctors.

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## Biomedical Informatics

An often-cited definition of the area has been proposed by Ted Shortliffe: *The rapidly developing scientific field that deals with the storage, retrieval, and optimal use of biomedical information, data, and knowledge for problem solving and decision making. It accordingly touches on all basic and applied fields in biomedical science and is closely tied to modern information technologies, notably in the areas of computing and communications.* Many areas have been established, including topics such as decision support systems, electronic health records, hospital information systems, data and text mining, information retrieval, bibliographic systems, medical imaging, etc.

Over the last 20 years, new areas have been introduced, such as merging medical informatics with bioinformatics, into what is called biomedical informatics. Then, areas such as translational bioinformatics have emerged. Fundamental topics include Web-based applications, the introduction of social networks, biomedical ontologies, semantic interoperability, Big Data research and others.

Whereas the GIB has worked in various of these topics, the group has intensively participated in pioneering two challenging areas:
(1) nanoinformatics, a new field at the intersection between informatics and nanomedicine and nanotechnology, and
(2) educating health professionals in Africa in various áreas — e.g., evidence-based medicine, biomedical informatics — through the use of advanced information technologies such as Web 2.0 applications and e-learning.

In 1994, the GIB began his long term involvement with Internet-based medical informatics research. Various projects related to topics such as heterogeneous database integration, protocol-based decision support, expert systems, data mining, image processing, visualization and analysis, surgical planning were started at the time. Such focus on Internet-based activities was awarded one of the five grants of the HISE (Health Information Strategic Initiative, by Hewlett-Packard, with groups from Harvard-MIT, Columbia, Berlin and UCLA)
This grant facilitated a first-class infrastructure for the group, whose developments began at this moment. In the last two decades, the GIB has reported publications in the most important conferences in the field, as well as journals such as The Journal of the American Medical Informatics Association (JAMIA), Journal of Biomedical Informatics, Methods of Information in Medicine, BMC Bioinformatics, Bioinformatics, BMC Medical Informatics and Decision Making, Nature, JASIST, Pattern Recognition, Pediatric Research, International Journal of Nanomedicine, Computing, Journal of Internal Medicine, Expert Systems with Applications, Computers in Biology and Medicine, Computer Methods and Programs in Biomedicine and others.

## Collaborations

The GIB has participated in many R&D&i activities. International collaborations began with the Decision Systems Group, from the Harvard-MIT Health Science and Technology division, led by Profs. Bob Greenes and Lucila Ohno Machado. A total of six researchers participated in this exchange at Boston. This collaboration has been extended to other US institutions such as Rutgers University (Prof. Casimir Kulikowski), Georgia Tech (Prof. Norberto Ezquerra), the University of Utah (Profs. Joyce Mitchell and Julio Facelli), hospitals and universities, with the participation in many joint projects and activities, including technology transfer.

In 2011, Prof. Maojo was elected a Fellow of ACMI, the American College of Medical Informatics, for his contributions to the area of medical informatics.

## Software Development

We have developed a large number of software systems, for companies, hospitals or as a result of our R&D activities within 11 European Commission projects and around 20 national projects:

1. ONTOFUSION: a number of tools for heterogeneous database integration
2. Brokerage Service (applied for Mobility and Training)
3. OntoDataClean: for data mining
4. BIRI and eMIR2: inventories of resources: for storing and accessing remote software tools
5. Protocol manager: multimedia tools for practice guidelines and protocols
6. Vocabulary server: for managing biomedical ontologies and terminologies
7. Mapping tool: for semantic integration of terminologies and ontologies
8. SIAC: an expert system for medical emergency management
9. Clinical trials manager: for managing clinical trials on cancer
10. Gene-Pdf: to convert contents of pdf files containing genetic information
11. Open PACS builder: a system for building small PACS
12. Numerous Web services and software tools for image processing, visualization, data management and text and data mining
13. A database for organ transplantation management
14. A software tool for remote collaborative work
15. Peer to peer image exchange tool
16. Geographical Information System linked to hotel reservations
17. An e-learning tool, for distance training
18. The Africa Build Portal, a social network for African health professionals
19. PubDNA finder
20. CDA Pubmed, a tool to link electronic health records to the literature
21. Spanish MeSH browser for Pubmed
22. A nanotoxicity search tool
23. A tool for automatically detecting shapes on nanoparticles

## Overview: The UPM

The Universidad Politécnica de Madrid (UPM, http://www.upm.es/), a top quality academic establishment with more than 3.000 faculty members, around 30.000 undergraduate students and 6.000 postgraduates in 21 Schools, has a strong commitment to R&D and Innovation. Within the 6th Framework Programme, the University took part in 149 European R&D projects with more than 25 M€ of funding received from the European Commission.

Within the 7th Framework Programme the UPM was recognized as the Spanish university with the highest numbers of projects approved and a leading European university. The UPM focuses on Engineering and Applied Sciences. In the last two years, various degrees have been introduced in the UPM curriculum: an engineering degree in biotechnology and another degree in biomedical engineering. The latter also includes an intensification in biomedical informatics in its fourth, last year.
The UPM is distributed over several campuses. One of them is located in Montegancedo, within the Urbanización Montepríncipe, which gathers the School of Computer Science (Facultad de Informática) and various research centers, with particular emphasis in biomedical topics.

Within the Montegancedo campus where the GIB facilities are located, there are various advanced Information Technologies (IT) infrastructures, such as a virtual reality cave, a wind tunnel, a living lab, advanced neuroscientific systems and the fastest supercomputer in Spain (CESVIMA). In the last Shanghai rankings of universities, the UPM was ranked in the top of Spanish universities in the area of computer science.

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## The GIB

The Biomedical Informatics Group (GIB) was formally established in 1993 under the direction of Professor Victor Maojo, a faculty member of the Department of Artificial Intelligence at the School of Computer Science. One year later, Prof Jose Crespo, a PhD graduated from Georgia Tech, joined the group. Built from scratch, the group is now a top Spanish group, in terms of top-ranked scientific publications, international collaborations and projects in the area of biomedical informatics. It is a reference in many research, educational and innovative European activities in the field.

The GIB's main interests are two: first, to carry out research in the field of biomedical informatics and second, to train young researchers in this interdisciplinary area, working on research projects and software development.

The GIB has more than thirty researchers and a large number of collaborators. We have participated in various research projects and networks, both national and international, particularly funded by the European Commission. For instance, the projects BIOINFOMED, INFOGENMED; INFOBIOMED, ACGT, Action-Grid, DICODE, P-Medicine, Integrate, EURECA, INBIOMEDVision and AFRICA BUILD. We have also carried out many research activities with various foreign and national hospitals and transferred R&D achievements to the Spanish industry.

Recently, the GIB has agreed to be part of the New Institute of Research, Hospital 12 de Octubre, in Madrid.

## Madrid: The City

Madrid is one of the most fascinating cultural cities in the world. Three museums (Prado, Thyssen-Bornemisza, Reina Sofía) make Madrid one of the prominent artistic cities in the world.

Miguel de Cervantes was born and lived in Alcalá de Henares, a city near Madrid. Other classical close cities are Aranjuez, El Escorial, Segovia, Toledo and Avila. Placido Domingo, born in Madrid, has been a cultural ambassador of the city over the last five decades.

Real Madrid, the top winner of football and basketball European cups, attracts every year millions of soccer fans.