

## New challenges for Bioinformatics and Computational Chemistry in NanoBiotechnology

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### Abstract

After the progress made during the Genomics Era, Bioinformatics was tasked to support the first flow of information generated by Nanobiotechnology at the early stages of development. This challenge requires the adaptation of classical bioinformatics tools, and also computational chemistry tools, to store, standardize, analyze and visualize the information generated in Nanobiotechnology. Therefore, bioinformatics and computational chemistry have been merged to develop a new sub-discipline called Nanoinformatics. This review depicts some new requirements such as the development of new tools and technologies that are critical for the design, modeling, simulation and visualization of Nanosystems that arisen during the accelerated evolution of Nanobiotechnology applied in life science. The knowledge obtained at the nano-scale implies the answer of new questions and the development of new concepts in different fields. Thus, it requires the implementation of collaborative networks and the creation of web platforms for sharing and discussing the knowledge generated in nanobiotechnology. For instance, the implementation of new databases schemes suitable to storage and to process data generated in nanobiotechnology (physical, chemical and biological properties of nanoparticles), will be key elements to derive the information needed to unleash the promise behind this convergent field. Therefore, in this work, we will also review some applications of Nanobiotechnology in life science, discussing how this application can generate new requirements for diverse scientific field such as Bioinformatics and Computational Chemistry.

**Keyword:** Bioinformatics, Molecular Simulation, Nanobiotechnology, Nanoinformatics, Nanomedicine.

## 1. INTRODUCTION

Richard Feynman introduced Nanotechnology as a concept in 1979 during a conference that took place at the California Institute of Technology. In that conference, Feynman gave the anticipatory talk “There is plenty of room at the bottom”, suggesting the idea about manipulating individual atoms and molecules, thus allowing the production of materials at the nanometer scale with promising technical, industrial and biological applications (Drexler, 1992). This conference and their derived material would be later considered as the theoretical starting point for the development of nanotechnology. Since then, nanotechnology has created a revolution not only in the fields of physics, chemistry, materials science, engineering, environmental sensing, manufacturing, and quantum computing but also with across-the-board applications in Clinical Research and Biotechnology. Consequently, new initiatives have created an international focus on new synthesis strategies, structures, phenomena, and properties associated with dimensional length scales residing between 1-100 nm (Tomalia, 2005). In this review, we will provide an overview about different nanotechnology platforms and some of their applications in life Science.

Although many strategies have been applied in order to advance in nanotechnology, a new approached based on the organization, interpretation, and prediction of the structure and physical-chemical properties of nanoparticles and nanomaterials, is starting. In general terms, the application of computer technologies, information science and molecular simulations have arisen as key methodologies to Nanobiotechnology and Nanoinformatics research; these methodologies are suitable to produce qualitative concepts, insights and design suggestions. While Bioinformatics is usually applied in the context of using computational tools to analyze DNA and protein sequence data, Nanoinformatics is applied in the context of characterizing particles and materials with application in nano- and biotechnology, by modeling and simulating them at the atomic level using computational chemistry strategies. In this article we will also discuss about the use of Nanoinformatics as a tool to understand nanotechnology applied in biological sciences.

The introduction of new techniques like this may accelerate the development of highly specific biomedical treatments, increase their efficiency, and minimize their secondary effects, among other applications. Introducing foreign bodies into the complex machinery of the human body is, however, a great challenge. In this context emerge the Nanomedicine concept, which during the last 5 years has grown very fast. A simple analysis of the number of links related with the term “Nanomedicine” has shown an exponential growth.

Computer-aided methods are the natural option to speed up the development of innovation in life sciences. However, new procedures for annotation and simulation of nanoparticle properties should be developed and analyzed in order to determine the limitations of computational methods applied in this field.

Medical applications of Nano, focused the attention of society in recent years. The first nanomaterials designed for biomedical sciences was done in 1985, and from the year 2004, the term “Nanomedicine” was widespread used. So far, the emergence of the modern Nano-biomedical sciences is dominated by the

convergence of applications towards biomedical problems, such as technologies product of breakthrough synthetic methods in lipid (liposomes), polymer (dendrimers) and colloid chemistry (metal colloids) and the discovery of entirely new chemical processes like fullerene and quantum-dot synthesis methods. All these new molecular systems have potential applications in diagnostics and therapy.

The lack of a common language as a mechanism for sharing knowledge is a huge impediment, especially in new disciplines. In an article titled “Nanomaterial Data Remain Scarce”,(Erickson, 2009) Dr. Britt E. Erickson explained that company participation in EPA's voluntary Nanoscale Materials Stewardship Program (NMSP) remains low, according to an interim report released by EPA on Jan. 12, 2008. EPA launched NMSP in January 2008 and gave companies the option of joining a basic program, in which they would submit only information that they already have about their nanoscale materials, or a more in-depth program, in which as time passes by, they would provide additional information, such as exposure, fate, and transport data. The program had a weak start, and although participation has improved since the six-month mark, the number of companies participating is still about 10 times less than EPA had predicted. As of Dec. 8, 2008, 29 companies had submitted information on 123 nanoscale materials under the basic program, and only four companies had agreed to participate in the in-depth program. EPA and the chemical industry consider the program successful, but critics argue that the poor participation underscores the need for mandatory reporting and testing of these materials.

These results emphasize the need to use Federated/governmental/etc databases, in order to organize and/or develop joint dictionaries and ontologies so that the data can be collected in a more meaningful way. On the other hand, the nature and the amount of new data from nanotechnology require GRID tools. Multi-scale datasets (from eM histopathology to molecular descriptors) are massive (15Tb with current technologies) and the analyses using combined data from multiple sources can only be achieved in a distributed environment, like GRID systems. The only realistic way to operate with this huge amount of information that could be combined in the near future with genomics information, is in a Federated environment with mix data models (public/private data etc.).

The next stage of this area probably will request funds for a focus study, in order to explore collaborative mechanisms for concept development and annotation that should include shared dictionaries and thesaurus generation.

## **2. CONVERGING TOWARD NANOBIO TECHNOLOGY AND NANOMEDICINE**

This section describes some of the new requirements emerged during the accelerated evolution of Nanobiotechnology. Requirements such as the development of new tools and technologies (e.g. new databases, and storage systems adapted to process information generated in Nanomedicine) will be critical for the design, modeling, simulation and visualization of nanosystems applied in life science. As suggested before, the new data

and knowledge obtained at nano scale imply the development of new ontologies (nano-ontologies), to achieve a conceptual consensus of all information, terminology and methodologies used in this field.

Nowadays, Nanomedicine has branched out in hundreds of different directions, each one of them is developing the ability to manipulate the structure and devices at the molecular scale, which can bring enormous and immediate benefits to the medicine (ETP Nanomedicine, October 22, 2009; Freitas, 2005). These applications are being focused on the treatment, monitoring and diagnostics in the new methods for drug administration and control of biological systems (ETP Nanomedicine, October 22, 2009; Farokhzad & Langer, 2006; Thierry, 2009).

Many resources and economic efforts have been used to develop new technologies in nanomedicine to reduce the mortality rate, morbidity that illness imposes to a patient, the prevalence of the disease and general social burden (ETP Nanomedicine, October 22, 2009). The growing interest in nanomedicine and the exponential generation of data at nano-scale allowed that interdisciplinary groups work together to create new nanoparticles with biomedical application. These data require an exhaustive analysis of their physical - chemical properties and an extensive structural characterization (ETP Nanomedicine, October 22, 2009; Farokhzad & Langer, 2006), which involves an intensive use of computational resources. For these reasons, nanoinformatics emerged to satisfy the need to develop computational tools, able to support the analysis of information generated each day in nanomedicine (García-Remesal et al., 2007; Gonzalez-Nilo Danilo & Cachau R., 2008; Iglesia et al., 2009). Nanoinformatics was supported in a first stage by US National Science Foundation (de la Calle et al., 2009) and other several international initiatives such as Action-Grid project. Another research initiative useful in nano-medicine is the BioInformatics Resource Inventory (BIRI). The BIRI is an approach for automatically discovering and indexing available public bioinformatics resources, using information extracted from the scientific literature. This tool is based on a domain-independent approach (De la Calle, Garcia-Remesal & Maojo, 2008; García-Remesal et al., 2007), that can be used to create inventories targeting different scientific fields. For now, this approach is currently being applied in the European commission-funded Action Grid project (Action-Grid project. Portal)

Thus, nanomedicine is a new coming field gathering the applications of nanotechnologies to healthcare (ETP Nanomedicine, October 22, 2009). This field is led by several expert groups in Europe, such as the Nanomedicine group of the Observatory for Micro-Nano Technologies (OMNT) ([www.omnt.fr](http://www.omnt.fr)) in France, the European Technology Platform (ETP) Nanomedicine ([www.etp-nanomedicine.eu](http://www.etp-nanomedicine.eu)), several cluster meetings organized by the European Commission on Personal Health Systems or on Micro-Nano-Bio Convergence Systems, and some European networks such as Nano2life (<http://www.nano2life.org/>) and ACTION-Grid (<http://www.action-grid.eu/>).

As from the necessity to extract, process, analyze, evaluate and visualize the information generated in nanomedicine at clinical level, new requirements have emerged for Biomedical Informatics (BMI). These new

challenges will be resolved through the use of nanoinformatics and the convergence technologies (NBIC)(Proyecto NBIC; Rodriguez, 2008), specifically the Information Technology and Communication Technologies (TICs).(Sommerfeld et al., 2009; Talbi & Zomaya, 2007)

At the same time Bioinformatics (Databases/-Omics) and Computational Chemistry approach (Design/Modeling/Simulation) can be used for evaluations of nanosystems used for nanomedicine in therapy and diagnostic. Initially, this area was unexploited due to the complex nature of biological, and pharmacological systems, and also due to the expertise and interdisciplinary efforts required to the formulating of computational models for complex phenomena at nano scale (Tentoni, 2003).

The application of nanosystems in personalized medicine, such as Drugs Delivery Systems, nanosystems for diagnostic and nanosystems for therapy, requires the development of computational tools and methodologies for its modeling and simulation. Additionally, implementation of strategies to interpret the information generated after the interaction of specific organisms with these nanosystems.

Recent studies (Milanesi et al., 2009) have established a scheme where all the components mentioned before converge around the study of a Biomedical complex system (see Figure 1). From all these complex systems emerge several nanotechnological research lines applied in Health, which may provide news ideas and concepts for solving pathological mechanisms and lead to novel therapeutic orientations.

### **3. NEW CHALLENGES FOR BIOINFORMATICS AND COMPUTATIONAL CHEMISTRY IN NANOBIOTECNOLOGY.**

Computational approach is important in the early stages of a project development to nano-scale. It can be used as a predictive technique in process to design nano-transport systems for a specific drug or molecular devices (Tentoni, 2003; Thierry, 2009). Nowadays, large molecular systems are being used as vehicles or transportation platforms because they can be modified with various chemical groups, which confer solubility, affinity and selectivity for specific sites of a cell (Kang et al., 2009; Tentoni, 2003; Thierry, 2009)

In recent years, computational molecular design has become an increasingly important field in research of new nanomaterials (Rickman & LeSar, 2003), this as result of the increase of the calculate capacity and the consolidation of a number of methodologies of computational chemistry (Gao, 2001)

Computational chemistry is a powerful tool to design, modeling, simulate and visualize of nanomaterials (Gao, 2001) and nanoparticles, such as dendrimers (Belting & Wittrup, 2009; Diekmann & Lindhorst, 2002; Newkome & Shreiner, 2007; Selim & Lee, 2009), metallic nanoparticles (Lee et al., 2009c; Murali Mohan et al., 2009; Prasad & Jha, 2010), nanocapsules (Fan & Hao, 2009), nanospheres (Lee, Yang & Holloway, 2009a), and quantum dots (Kang et al., 2009). These nanoparticles are being used in nanomedicine as carriers, sensors and

systems for early diagnosis of diseases (Belting & Wittrup, 2009; ETP Nanomedicine, October 22, 2009; Kang et al., 2009).

Computer-assisted nanomolecule design has emerged from recent advances in computational chemistry and nanotechnology and is considered well suited for assisting to the experimental community in the design of new nanostructures (Bewick, Yang & Zhang, 2009). The major advantage of computational nano-design is that it provides a relatively inexpensive and fast way to explore many structural designs, including the study of stability and prediction of properties (Shapiro et al., 2008).

The application of modeling methods and nanoscale simulation to the nano-design demands new methods or the adaptation of the techniques used in computational chemistry, such as classical molecular dynamics simulations (Fermeglia & Pricl, 2009; Gates et al., 2005), molecular mechanics (Shapiro et al., 2008) and quantum mechanics (Gates & Hinkley, 2004; Shapiro et al., 2008). Besides the use of these computational methods at atomic level, it is necessary to implement new approaches in the use of quantitative structure–activity relationships (QSAR) studies in this field (Shapiro et al., 2008).

The Computational Chemistry using molecular dynamics (MD) in nanostructures, requires a good characterization of the physical and chemical properties (Shapiro et al., 2008), with the purpose of obtaining accurate simulation results about the structural and dynamics properties of nano-systems at atomic level (Gates et al., 2005). In general, the nanosystems are amorphous, and then the use of molecular modeling tool is a critical to this task. CNS (<http://nanobiology.utalca.cl>) is the first initiative in the world that includes a database of structure of nanoparticles. The first state of this initiative includes more than 120 of different models of dendrimers that were build using advances molecular simulation techniques. CNS is an initiative of SAIC-NCI, USA, in collaboration with CBSM-UTalca from Chile.

Computational Chemistry using molecular mechanics (MM) can be used to determine the optimized structure of nanoparticles or nanomaterials (lowest energy conformation). This is based on a model of molecules where spheres describe the atoms and springs represent the bonds between the atoms (Gates & Hinkley, 2004). The total energy of the molecule is calculated as the sum of energies implemented in a particular force field (energies of stretching, angles, torsion, VdW interactions, electrostatic interactions and hydrogen bonds) (<http://www.charmm.org/html/documentation/c34b1/energy.html>). Thus, modeling at nano scale requires force fields that are sufficiently accurate for both the inorganic and organic components of the nanostructures. These features are extremely important for determining the 3D structural characteristics of nanostructures.

Computational chemistry also use quantum mechanics (QM) such as semi-empirical, *ab initio* and density functional theory (DFT) to predict the molecular structure at electronic level of nanomaterials and compute different molecular descriptors that depend of the electronic configuration of the system (Shapiro et al., 2008). These methods, are not only limited by the number of degrees of freedom, but besides due to the time scale that require this kind of calculations (<http://www.charmm.org/html/documentation/c34b1/energy.html>;

Shapiro et al., 2008). For this reason, the application of QM methods to nanoscale simulation for nanodesign demands new methods or the adaptation of the techniques used traditionally.

Several studies have been carried out using a cycle based on theoretical and experimental studies, with the aim of achieving a better understanding of systems at nanoscale. For example, Haddish-Berhane *et al* (Haddish-Berhane, Rickus & Haghghi, 2007) have studied multiscale framework to integrate current computational approaches at different scales for drug delivery problems based in nanoparticles (Figure 2). It is expected that about 30% of pharmaceutical expenditure will be based on computer simulation, through an integrated effort between experimental and theoretical groups.

Theoretical models used for the design of different nanoparticles are diverse and use different approaches well developed during the last 40 years in computational chemistry. For example, Deduzzi et al (Lee, Ferrari & Decuzzi, 2009b) have developed a theoretical study about size, shape and surface of nanoparticles using modeling techniques. Such features seem to play an important role when used as carriers and sensor systems in the intravascular journey.

Another example in this subject is the study carried out by Pillay et al (Sibeko et al., 2009), where it was employed advanced computational tools to design a drug delivery system based in biopolymeric membrane. Specifically, it was studied the influence of triethanolamine on the release properties of methotrexate from a composite biopolymeric membrane. Properties such as drug entrapment efficiency and the mechanisms of drug delivery have an important impact on the design of these kinds of systems. These properties require a deep study and characterization at molecular level. Thus, the designs of new nano-devices require the use of advanced computational tools in order to accelerate the understanding of the action mechanics of the drug delivery.

Therefore, the need for accuracy and speed in the design of nanostructures requires the development and implementation of new computational chemistry methodology or adaptation of existing methods for generating of workflows and different protocols to design with the aim of creating nanostructures that suit their physical and chemical properties.

#### **4. MOLECULAR SIMULATIONS: KEY TECHNIQUES TO UNDERSTAND FUNDAMENTAL PHYSICOCHEMICAL PROPERTIES OF NANOPARTICLE.**

Simulation techniques have been widely used to model a variety of phenomena, being the general approximation to treat the interacting particles as rigid spheres connected by springs (Fig. 1, Panel 2). More recently, the development of force fields (Daggett, 2001; MacKerell, Banavali & Foloppe, 2000; Ponder & Case, 2003) suitable to perform biomolecular simulations, permitted the study of diverse atom-level biological systems, ranging from a couple thousands atoms (Artigas et al., 2008a; Barria et al., 2009; Gogonea et al., 2001; Gonzalez et al., 2008; M. J. Frisch, 2004), up to the whole-organism level, with the recent modelling report of

the complete TMV virus (Freddolino et al., 2006). Force fields used for biomolecular simulations (Case et al., 2005; MacKerell et al., 2000), as like as CHARMM and AMBER include both bonded and not-bonded interactions between all the represented atoms, plus expressions to model the effect of Van der Waals and Coulomb potentials, incorporating on the system's trajectory long-range effects induced by mass and charge, respectively (Daggett, 2001; MacKerell et al., 2000).

In spite of the validity for the mathematical expressions that compose the available force fields, parameterization constants are included in all the bonded and not-bonded terms (see Fig. 1). These constants are fine-tuned using either pure quantum mechanics calculations (*ab initio*) or empirically-based approaches (Ponder & Case, 2003). When compared with wet-lab experiments, molecular simulations results have proved to be as accurate as typical experimental methods like microcalorimetry (Patra & Karttunen, 2004; Ponder & Case, 2003; Price & Brooks, 2002). Thus, molecular simulations based on force fields have become a popular methodology to explore the behaviour of biomolecules at all the micro, meso and nanoscale.

As denoted before, molecular simulation techniques depend on the structure of the biomolecular system to be modelled. So, much attention has being paid to develop databases to contain molecular structure data. Since the primordial research efforts dedicated to produce crystallographic structures of biomolecules in the decade of the 70's, public databases such as Protein Data Bank ([www.pdb.org](http://www.pdb.org), Rutgers University, The State University of New Jersey and the University of California, San Diego, USA), compile more that 62.000 biomolecular 3D structures (near to 35.000 unique structures). However, the growth of unique folds at PDB and the results of international joint efforts as the Structural Genomics Project (Lundstrom, 2007; McGuffin & Jones, 2002; Sali, Lima & Kostic, 2007), demonstrate that we know only a proportion of the different architectures and macromolecular arrangements in the human body. Moreover, the complexity of the intracellular environment complicates the crystallization for many proteins. As a consequence, membrane integral proteins such as channels and other transporters are usually under-represented in databases as PDB.

Based on a seminal work from the decade of 80's that demonstrated that the structure is more conserved than sequence (Chothia & Lesk, 1986; Chothia et al., 1986), new methods to produce molecular models based of reference structures were developed (Sali & Blundell, 1993; Sali et al., 1995; Sanchez & Sali, 2000). These methods, commonly known as comparative modelling techniques, are suitable under some restrictions, to produce models able to be used as sources for protein engineering (Colombres et al., 2008; Eyzaguirre et al., 2004), computer based drug design (Lagos et al., 2008; Lizama et al., 2009; Vasquez et al., 2007), to explore structure-function relationships (Artigas et al., 2008b; Barria et al., 2009; Carvajal et al., 2003; Ehrenfeld et al., 2008; Stange et al., 2008; Strobel et al., 2005; Tischler et al., 2005), and to explore signal-transducing mechanisms (Gonzalez et al., 2008; Inestrosa et al., 2005; Strobel et al., 2004), among a variety of applications.

Extensive efforts have been made to characterize, at the experimental level, the fundamental physicochemical properties of nanoparticles with potential applications in biomedical sciences. However, all

these efforts have faced the limits of current experimental techniques, because the “nanoscale” has proven to be too small for light microscopy, while too amorphous for x-ray crystallography, too heterogeneous for NMR and too ‘wet’ for electron microscopy (Lu et al., 2006). Under these circumstances, molecular modelling and simulation techniques have arisen as key methodologies to Bio-Nanotechnology research, suitable to produce qualitative concepts, insights and design suggestions. Thus, quantum mechanics, molecular modelling and molecular simulations techniques provide representations of nanosystems at the atomic level with electronic resolution, offering a suitable framework for the characterization of diverse nanosystems’ physical-chemical properties. Advancing in these efforts, the report of several molecular dynamics (MD) simulations of nanoparticles and other nanosystems demonstrated the suitability of these computer-based techniques to explore and understand basic properties of nanoparticles and nanomaterials (Cieplak & Thompson, 2008; Khurana et al., 2006; Martin, Zhu & Krilov, 2008; Zimmerli & Koumoutsakos, 2008). Moreover, these tools provide a unique source of information not only to model basic nanoparticles properties, but also to gain insight into the interactions with biological systems. The application of computer-intensive methods like hybrid quantum mechanics and molecular dynamics (QM/MM) simulations, enriched with proper algorithms to efficiently sample the vast conformational space, will permit the characterization of a wide variety of nanoparticle properties, obtaining insights into the biological phenomena that commands nanoparticles recognition by physiological systems (Arayne, Sultana & Qureshi, 2007; Archakov & Ivanov, 2007; Bianco, 2004)

As indicated in the previous sections, the impact of Molecular Modelling and Simulations in Nanotechnology has being notorious during the last decade. Molecular modelling and simulations offer a unique way to explore interactions at different scales that range from thousand of atoms, to even millions of them. Through these simulations, fundamental physicochemical properties of nanoparticle and other nanoscale systems can be studied. The ever-increasing computer capacity of supercomputers together with a systematic price reduction will allow the expansion of molecular simulations to different nanotechnology fields. New ways of human-computer interactions as haptic devices, complemented with nano-lithography and directed synthesis, will allow the atom-by-atom design of nanoscale systems. Atom-by-atom design expands the creative freedom in the creation of nanoparticles, enabling the obtention of unique properties. However, the same freedom used to create these nano-scale aggregates without the constraints imposed by the use of standard components (i.e., chemical functional groups, amino acids, nucleotides, etc.), makes the identification of the intermediate complexity modules, that give raise to the nanoparticle's peculiar properties, a real contemporary and currently unsolved challenge. Nanoinformatics as a whole, comprising by the vast set of computer-related tools to design, store and analyse nanotechnology data will emerge in the near future, as a promising application to the same old reliable set of tools.

## **5. DEVELOPMENT OF COLLABORATIVE NETWORKS PLATFORMS FOR NANOBIO TECHNOLOGY.**

### **5-a. Design web portals**

To facilitate data sharing (recent literature, tutorials, papers, links and access points to nanomedical database; jobs and news, updated daily) in the research community to expedite and validate the use of nanoparticles, nanomaterials and nanosystems in nanomedicine (ETP Nanomedicine, October 22, 2009; Gordon & Sagman, 2003). Nanowerk Nanotechnology Portal (<http://www.nanowerk.com>), NanoLink (<http://www.nano-link.net>) and CaNanoLab (<http://cananolab.abcc.ncifcrf.gov>) are clear examples of portals dedicated to promote the information generated in nanomedicine and nanotechnology in general. The first one is a portal with great variety of links and directories about nano research, daily news and nanotechnology feature articles, reports, events calendar and a nanomaterial database focused on nanomedicine and nanoelectronic (NanoLink is a portal web)]. The second portal pursuing life quality through technological innovation (LINK=Life quality through Innovation by a Network of Knowledge). NanoLINK will be a consolidated network of networks focused on nanotechnology (nanoLINKnet) (Nanowerk Nanotechnology Portal). CaNanoLab is also a portal web focused to promote the dissemination of nanobiological information across the scientific community (The cancer Nanotechnology Laboratory (caNanoLab) Portal).

### **5-b- Implementation and maintenance of forums**

As a platform of interactive communication to discuss the new possibilities offered by nanotechnology in medicine and promote thus the process of transfer of technology and information among different areas of science, health, pharmaceutical industry, education, among other areas, sustained through the nanoinformatics. Several examples for that are: the Nanoforum (<http://www.nanoforum.org/>), NanoNewsBoard Forum (<http://www.amtexpo.com/nano/>) and the Institute of Nanotechnology Forum (<http://www.nano.org.uk/forum/index.php>). The first one was developed by the European Commission through FP5 with the purpose of disseminate the advances of different areas explored by nanotechnology, including of course the development of nanomedicine, its current outlook and its projections based on the successful discussion of research to nano-scale (Funding and Support for International Nanotechnology Collaborations Nanoforum report, December 2005). The second, NanoNewsBoard is a nanotechnology forum sponsored by access multimedia technology Inc (USA) (NanoNewsBoard) and the third forum was implemented by the Institute of Nanotechnology (IoN-UK) (Institute of Nanotechnology Forum), both contains information related with different topics in nanotechnology news, including nanomedicine (ETP Nanomedicine, October 22, 2009).

These forums allow users to be updated with the latest advances in the use of nanotechnology applied to medicine.

### **5-c. Development of thematic networks and collaboration.**

On nanotechnology, with the aim to have a space dedicated to facilitate the interaction among the professionals (Collaboration between groups with different expertise and resources (technical, scientific, social and political) that are working at the intersection between the information obtained from biomedical and health areas to nanoscale (Funding and Support for International Nanotechnology Collaborations Nanoforum report, December 2005; Gonzalez-Ibanez, Gonzalez-Nilo & Cachau, 2009). In order to share (Open access and dissemination of data and tools i.e. Open Source), to promote and improve standards of biomedical information generated across the nano-scale (Nanohub Forum; National Institute of Health (NIH), 2006) and allow users anywhere in the world an easy access to information. Examples for current thematic network and collaboration are: The Collaboratory for Structural Nanobiology (CSN) (<http://csn.ncifcrf.gov/csn>), The nanoHUB (<http://nanohub.org/>), and NanoMedNet (<http://www.nano.org.uk/nanomednet/>). The First is a nanobioinformatic web service dedicated to collection, curation and correlation of structural, physical-chemistry, biological and biomedical data (The Collaboratory for Structural Nanobiology (CSN)). The second is a web platform for research, education and collaboration in nanotechnology (Nanohub Forum). The third, NanoMedNet is a collaboration web platform that promotes information of various aspects of the emerging field of nanomedicine, develop further services and tools and develop the education and training of medical professionals that are related with the field of nanomedicine (NanoMedNet ).

### **5-d Creation of storage systems and data exchange.**

The large increase of data and information generated through measurement or calculations of physical and chemical properties of nanostructures and nanomaterials (The cancer Nanotechnology Laboratory (caNanoLab) Portal), mathematical models from clinical nanomedicine (Bewick et al., 2009), taxonomy of nanomedical application (Gordon & Sagman, 2003), nano-ontologies (The cancer Biomedical Informatics Grid (caBIG)), high throughput experimentation/discovery (Tentoni, 2003), tools for visual analytics of nanoimages (Mauger et al., 2007) and data mining of biomedical data (Zweigenbaum et al., 2007), require the creation and implementation of systems and tools for sharing and storing this information.

The creation of databases or repositories (Database of Nanoparticles; Mauger et al., 2007; Sommerfeld et al., 2009) to allow the exchange of information about the 3-D structural and data of physical and chemical properties of nanoparticles with biomedical applications, such as dendrimers, nanotubes and metal particles,

quantum dots, among others, is critical to the multidisciplinary development of nanomedicine.

The Biomedical data are being generated at different levels; specifically, at atomic level (nanomedicine) has had an explosive increase (ETP Nanomedicine, October 22, 2009). This large flow of information requires of secure and easy availability storage systems. The current information storage systems, called data warehouses, can be expanded to the information generated in nanomedicine. Thus, the data warehouses (Sommerfeld et al., 2009; Staggers et al., 2008; Talbi & Zomaya, 2007) can be optimized through nanoinformatics tools and the technologies of information and communication (TICs) as store systems for nano-scale systems useful in medicine.

Several projects in this area have been developed, this is the case of the structural database CSN (Collaboratory for Structural Nanobiology, <http://nanobiology.utalca.cl>), The CaNanoDB (<https://gforge.nci.nih.gov/projects/canano/>) and The ICON EHS Database (<http://icon.rice.edu/research.cfm>). The first one is a structural database of various nanoparticles with possible nanomedicine applications. In this site can be find downloadable nanopdb files, related research data, and resources for visualization of different nanoparticles such as dendrimers, nanotubes and metallic particles (The Collaboratory for Structural Nanobiology (CSN)). The second, caNano Data base (CaNanoLab) includes all available technologies and a toolbox for modeling of targeted drug delivery and diagnostics using nanoparticles as transport platforms (The cancer Nanotechnology Laboratory (caNanoLab) Portal). The third project is a database that contains summaries (abstracts) and citations for research papers related to the Health and Safety implications of nanoscale materials (The ICON EHS Database ).

## CONCLUSION

During the last year bioinformatics and molecular simulations have evolved around biotechnology, but just a few examples shown a continuum analysis from genome to the protein structure. Now, the accelerated evolution of the convergence of Biotechnology and Nanotechnology pose new challenges and concept that require the rapid convergence between bioinformatics and computational chemistry. Therefore, concepts like Nanobiotechnology and Nanomedicine present a great opportunity to our community to merge concepts and tool developed during the last decades in computational chemistry and computational biology. Thus, requirements like database, storage, ontologies and annotation (bioinformatics) should be merged with design, modeling, simulation and visualization (computational chemistry) of Nanosystems, to generate a new sub-discipline called Nanoinformatics. Many of the applications of nanotechnology in Medicine and Biotechnology, reviewed in this work, require advanced approaches to manipulate nanoparticles at molecular level (nano scale) that are mixed with implementation of collaborative networks and the creation of web platforms for sharing and discussing the knowledge generated in Nanobiotechnology. For instance, the implementation of new databases schemes suitable to storage and to process data generated in Nanobiotechnology - connecting physical, chemical and biological properties of nanoparticle -, will be a key element to derive the knowledge needed to develop these new era, where the converging sciences will be the driving force of the development of new concepts, knowledge and technologies. The implementation of these new techniques may accelerate the development of highly specific biomedical treatments, increase their efficiency, increase their bioavailability and minimize their secondary effects, among other applications that should revolutionize the vision of the future development of medicine and biotechnology.

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**Figure Captions**

Figure 1. Scheme where is depict the convergence of different research lines from Biomedicine to Nanobiotechnology around biomedical complex system.

Figure 2: A framework for multi-scale modeling of drug delivery systems using information from drug and vehicle properties, disease pathology, and patient characteristics. Scheme adapted from Haddish-Berhane *et al* (Haddish-Berhane et al., 2007).

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Figure 1

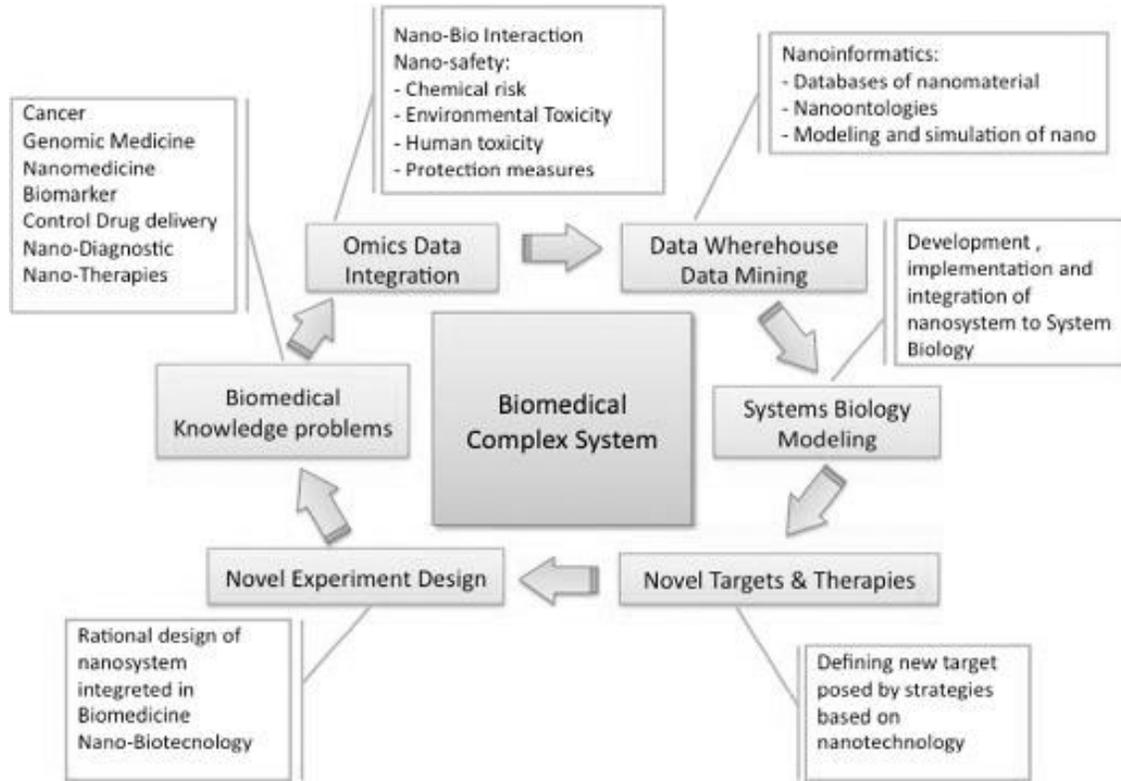


Figure 2

