Aligning Biomedical Informatics with Clinical and Translational Science

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Abstract
Clinical and Translational Science (CTS) rests largely on information flowing smoothly at multiple levels, in multiple directions, across multiple locations. Hence, Biomedical Informatics (BI) is seen as a backbone that can help to manage the information flows for the process of translation. However, the two concepts may end up being applied incongruently, if uncoordinated. This paper summarizes the objectives for CTS and BI, and provides a mechanism to harmonize their different objectives and guide the design of BI architectures for CTS.

1. Introduction
Clinical and Translational Science (CTS), as a new paradigm for the generation and use of new knowledge in medicine, expects to speed up the knowledge transfer process from silos of basic science to the clinical setting, and vice-versa, more rapidly and efficiently [1,2]. The current rate of success in translation is low and the process is time and resources consuming [3]. However, biomedical informatics (BI) can be used to reduce the time lag and optimize the use of resources.

In order to successfully implement and use BI for CTS, a platform capable of supporting the core activities in translation will be required – a platform that not only serves as technological support connecting databases, but as one that fosters the psychological, educational, and social experience as well as for information to cut across silos [4]. The importance of strategically planned infrastructures supporting information flows in CTS has been recognized; however, there is a gap in design studies to address the sound architecture of structures and processes for biomedical innovation [5].

The next section will synthesize the objectives identified from the literature for CTS and BI, followed by the analysis of how the technological approach can serve as a backbone for fast and efficient translation. We will conclude with final remarks and an agenda for future research.

2. CTS and BI objectives
The organization of medical research and practice for the production and application of knowledge has not been able to realize its full potential [1]. CTS needs to overcome critical impediments before the findings from the best science can be utilized in the day-to-day care-setting and the two-way collaboration between the bench and the bedside is established. Examples of the barriers for translation are the overuse of scientific jargon [6], need for measurement improvement [7], and the poor quality and availability of data collected at the bedside for scientific studies [8].

A bibliographic review allowed us to identify the main objectives for both CTS and BI. We describe those objectives in a way that their representation provides insights on how to boost the effectiveness of translation by using the BI approach in a CTS Center.

2.1. CTS objectives
The main goal of CTS is to achieve faster and efficient translation of knowledge [2] generated and stored in silos of basic science disciplines [9,10] into applications that reach the bedside and the community [11]. At the same time it seeks to generate new knowledge through basic research on problems discovered at the bedside [7]. Such knowledge would be materialized in the more effective and efficient production of drugs, treatments, diagnostic methods, medical devices and healthcare policy [7,12], and less expensive medicine for the community [7].

The key factors affecting fast translation identified in the literature can be categorized into the following five groups: (a) Level of multidisciplinary collaboration, (b) Probability of technical success, (c) Global impact of target diseases, (d) Availability of resources across silos, and (e) Compliance with established norms. Each cluster would impact translation positively by reducing barriers and creating

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necessary conditions for faster translation. Each group is described below, and then summarized in Figure 1.

2.1.1. Level of Multidisciplinary collaboration. Multidisciplinary research teams are a pillar not only to complement the use of skills and knowledge in biological research [8], but are also crucial for the implementation of translational ‘homes’ [5,13]. Facilitating interdisciplinary groups may include different modalities like giving appointments to translational scientists in different academic departments, putting clinical and basic scientists together in groups focused on a disease process, or providing platforms that help scientists to manage and enhance their social networks and participate in indirect networks [14]. Konagaya [15] describes a platform over the internet for sharing resources, knowledge and services in bioinformatics as a good tool to coordinate groups. However the study also reveals a semantic gap between the workflows and interfaces provided by web services. Such gaps are not uncommon in biomedical fields, and the establishment of ontologies that systematically describe genes, proteins, diseases, resources, etc., is needed [6]. Since multidisciplinary collaboration demands the participation of investigators from different scientific and practical domains, data and resources will be inherently heterogeneous [8], and the existence and use of standards and shared languages would better support collaboration between discovery and clinical scientists [11,16]. It is claimed that the expertise of an effective translational scientist can no longer be acquired on the job, but they should be formally trained in biomedical and behavioral sciences [12]. Also, to foster the recruitment of individuals, recognition for multidisciplinary research and incentives for career development will be fundamental [17].

2.1.2. Probability of technical success. Increasing the probability of technical success will happen only if the entire process of research and development is optimized and the bottlenecks minimized [18]. An optimized process of research and development not only depends on using new technologies, but also depends on an enhanced prediction and learning cycle between scientists and clinicians [19] that show effects on the right targets at the earliest stage possible [7]. Better probability of success would be achieved if BI can reduce barriers between the bench and the bedside (oversimplified assumptions about the human diseases, deficient measures, limited applicability to humans of animal models, scarce academic publication of negative results, information floods in scientific jargon, etc.), as well as barriers from the bedside to the bench (rare systematic collection and sharing of information with discovery scientists, heterogeneous data, data difficult to use in scientific studies, unfocused, biased, and of poor scientific standards clinical science, unsympathetic review process preventing publication of clinical studies, etc.). We assert that in order to increase the probability of technical success it will be necessary to improve the feed-forward and feed-back loops from bench to bedside, and bedside to bench [2], improve mechanisms to measure process and impact of drugs [7], identify good animal models [2,9], and strengthen partnership between academia and industry to share resources and knowledge [20].

2.1.3. Global impact of target diseases. Translational science not only intends an improvement in the rates of success in transforming basic science into new healthcare products (preclinical research or T1), but also aims to reach the community with applications that significantly improve its health (applied clinical research, or T2) [11,21,22]. Under this logic, it is helpful to differentiate serious medical conditions with significant impact from low impact and less risky health problems; in this way, research could be focused on diseases with global impact and prioritize the maximization of social benefit in the long run [1]. It is also necessary to avoid major investment in the development of drugs and treatment for diseases that present null or non-significant impact [9] which in some cases become population needs due to good marketing and advertising techniques [1].

2.1.4. Availability of resources across silos. Faster translation requires that resources produced and stored in silos can flow [9] across basic, animal, human and public health research [10]. Biological information and resources are generated in large volumes, but in general, not systematically classified or indexed [6]. It is indispensable to have a dynamic catalog of resources and tools for translation that can be easily accessed [15]. Beyond a descriptive catalog, the opportune access to specific, relevant, complete, ranked and categorized information according to the interests of basic and applied investigators would also be of great assistance [10] if presented in an easy to navigate format [6] allowing effective communication of clinical and basic research outcomes.

2.1.5. Compliance with established norms. Health information of individuals can be sensitive and, if incorrectly managed, the exchange and sharing of such information could violate the confidentiality and privacy of individual’s medical information [23,24]. Guidelines are available to conduct ethical research in study design, data collection, analysis, sharing, and
disclosure of results [25-27], which should be followed not only during the design of studies and research, but it has been proposed that such practice should be required for academic publication in studies involving humans [27]. As part of the practical and scientific dynamics, translational science may foster the discussion of topics like biomedical data ownership [8], the effectiveness and applicability of current norms [26], or the plausibility of a universally available electronic medical record that reduce administrative costs in healthcare [24].

2.2. BI objectives

The objectives of a biomedical informatics service in the context of CTS are not only to provide a platform to share computer tools and digitized resources like databases or software, but also to create tools that help knowledge to cut across silos [13] supporting collaboration among scientists and practitioners [2,10]. This vision represents more than a technological platform, but a social and cultural, organizational, and educational change [4]. An information system to foster CTS should support the efforts to enhance the understanding of full time clinicians about scientific aspects, and to increase the understanding of basic scientists of the difficulty of dealing with humans [2]. We assert now that a CTS-BI infrastructure should not be only a technological infrastructure, but rather a service that make efficient and effective the generation, search, exchange, storage, retrieval and management of knowledge, computer tools and resources.

The objectives of the BI services have been clustered into five groups: (a) Provide access to resources and information, (b) Ensure robustness of the system, (c) Create environment for collaboration, (d) Retrieve relevant information, and (e) Protect the virtual environment.

2.2.1. Provide access to resources and information.

The flows of information (feed-forward, feed-back and feed-in) between silos are slow and in some directions rare – like the flux from bedside to bench [7,9]. One objective of a CTS biomedical informatics platform is to generate channels to exchange resources and to allow scientists and practitioners to access them. Such

![Figure 1. Institutional objectives for a CTS Center](image)
communication channels would represent an important tool to reduce the barriers and cut across silos where information and knowledge are generated and stored. Different methodologies, data, academic and applied studies and publications can be found in each silo. Such resources could be applicable in other silos, for example, data from human studies could be contrasted with animal studies to assess and improve animal models, or simulation techniques may be applied on data sets for different diseases to discover common patterns and biomarkers.

2.2.3. Create environment for collaboration. In order to create an environment that ‘inspire[s] good will, friendship and fellow feeling’ [28], several ideas can be implemented. One objective for the CTS-BI services is to make the search of information and bioinformatics tools easy-to-navigate [6]. A friendly computer environment will help scientists to access resources and manage their interactions with other investigators easily. The CTS-BI platform can be a common place to create, enhance and maintain social networks with scientists and practitioners, to share interests in virtual communities, and allow academic and non-academic discussion. Also, customized service could be provided if the profiles and interests of investigators are accessible.

2.2.4. Retrieve relevant information. Relevant information provided in ordered and proportioned manner can be key for people to be able to associate information to the questions they have [29]. Floods of information can overwhelm the attention of the user, making it imperative to select only the relevant pieces from the information superhighway [30] and elicit meaning from it. Consequently, an important objective of CTS service is to add value to search, for example, by presenting results ranked according to keywords [31] or other relevant criteria. Other ways to organize the resources are making dynamic catalogs of the tools and resources available [6], alerting investigators to relevant news, learning from their search history and profiles, and sending feedback from other users.

2.2.5. Protect the virtual environment: Virtual environments are vulnerable to attacks, failures or natural disasters that endanger the security and reliability of the service. The efforts to protect the virtual environment and make it trustworthy are indispensable. To protect the biomedical virtual environment, technical solutions can be helpful, like mirroring critical resources, backup important information, keeping updated versions of antivirus and properly configured firewalls. Other actions not purely technical, but practical will be necessary as well, such as avoiding intruders to gain access through social engineering, encouraging the use of strong passwords, avoiding the use of vulnerable software and applications, enforcing encryption for transactions involving sensitive information, validating users and their transactions and using de-identified biological data [24].

Figure 2 summarizes the BI platform objectives to support the institutional objectives of a CTS Center.

3. Objectives correspondence

A BI service supporting a CTS Center may require additional resources, but the main contribution of the BI to the CTS approach comes from a reorganization of the assets and cultural acceptance of a new structure to access and share resources [10] and knowledge.

Having identified the main organizational objectives for a CTS Center, and the objectives for the BI service, we analyze which BI objectives are critical to support the organizational objectives for the achievement of fast translation. This correspondence
technique not only allows the identification of key BI objectives, but also helps to see what organizational objectives are supported by BI, and what BI objectives may have null institutional impact. This analysis is a key first step in designing systems to avoid unnecessary redundancy and optimize the use of resources to support the strategy and operations of the CTS Center.

At the next level of detail, the correspondence between objectives and sub-objectives for the BI platform and the CTS Center, are contrasted on a one-on-one basis.

Table 1 presents a detailed description of objectives and sub-objectives correspondence. From the identified BI sub-objectives, to facilitate the access to studies and publications can help to:

- Organize data
- Prepare translational scientists
- Strengthen partnership with the industry
- Enhance feedback loop
- Identify good animal models
- Identify biomarkers
- Establish a hierarchy of diseases impact
- Study the impact of current healthcare programs

Create a catalog of resources
- Provide access to data
- Communicate results effectively

Then, to facilitate access to studies and publications becomes fundamental, but this is not a new function, it is in fact common and one pillar of good quality research to review literature; then the value depends on the attributes of the sources of information, like breadth, updated contents and access to it. Similarly, access to biological data and access to methodologies for analysis support most of the institutional goals and the objective provide access to resources and information can be considered key for faster translation.

Make catalogs of tools and resources available, alert relevant news, and add value to search help to:

- Organize data
- Coordinate teams
- Partner with the industry
- Augment feedback loop
- Identify animal models and biomarkers
- Create catalogs of resources
- Provide access to data
- Effectively communicate research results

Figure 2. BI platform objectives
<table>
<thead>
<tr>
<th>Organizational Objectives</th>
<th>BI Platform Objectives</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Access to resources and information</strong></td>
<td>Policies and rules to use CTS service</td>
</tr>
<tr>
<td>Access biological data</td>
<td>Use adequate technology</td>
</tr>
<tr>
<td>Access methodologies for analysis</td>
<td>Tools for social networking</td>
</tr>
<tr>
<td>Access studies and publications</td>
<td>Tools to manage communities</td>
</tr>
<tr>
<td><strong>Ensure robustness of the system</strong></td>
<td>Allow non-academic discussion</td>
</tr>
<tr>
<td>Prevent immunological challenges</td>
<td>Develop Scientists profiles</td>
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<tr>
<td>Continue multi-disciplinary efforts</td>
<td></td>
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<tr>
<td>Colleague data</td>
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<tr>
<td><strong>Create an environment for collaboration</strong></td>
<td></td>
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<tr>
<td>Organizational Objectives</td>
<td>BI Platform Objectives</td>
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<tr>
<td>---------------------------</td>
<td>------------------------</td>
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<tr>
<td>Foster multidisciplinary collaboration</td>
<td>Present relevant information</td>
</tr>
<tr>
<td>Organize data</td>
<td>Add value to search</td>
</tr>
<tr>
<td>Coordinate teams</td>
<td>Alert relevant news</td>
</tr>
<tr>
<td>Prepare translational scientists</td>
<td>Make catalogs available</td>
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<tr>
<td></td>
<td>Send feedback to users</td>
</tr>
<tr>
<td>Increase probability of technical success</td>
<td>Protect the virtual environment</td>
</tr>
<tr>
<td>Partnership with industry</td>
<td>Protect individual’s privacy</td>
</tr>
<tr>
<td>Enhance feedback loop</td>
<td>Enforce encryption of sensitive data</td>
</tr>
<tr>
<td>Identify good animal models</td>
<td>Mirror important information</td>
</tr>
<tr>
<td>Identify good biomarkers</td>
<td>Target global impact diseases</td>
</tr>
<tr>
<td>Study impact of current healthcare programs</td>
<td>Make resources available across silos</td>
</tr>
<tr>
<td>Comply with established norms</td>
<td>Create catalog of resources</td>
</tr>
<tr>
<td>Identify applicable norms</td>
<td>Provide access to data and studies</td>
</tr>
<tr>
<td>Define methods for data collection, sharing and ownership</td>
<td>Effectively communicate results</td>
</tr>
</tbody>
</table>

Table 1: Objectives and Sub-Objectives Correspondence for CTS and BI (Contd.)
Then, *presenting relevant information* from the superhighway of data becomes the second critical capability that a BI platform can provide to successfully translate science into applications. Additionally, a BI platform allowing non-academic discussion and providing tools to manage communities and enhance social networking can contribute to boost the level of multidisciplinary collaboration, increase the probability of technical success, expand the availability of resources across silos and to assess the global impact of target diseases.

The BI system objectives mentioned represent strategic and cultural challenges, and are seen in this paper as the most important factors that will trigger the change and speed up the process of translation.

To *ensure the robustness of the CTS-BI service* and to *protect the virtual environment* are necessary goals to achieve in order to comply with established norms, to protect privacy and to cultivate trustworthiness among the users of the system. Such characteristics not only rely on the technical design and implementation of technology, but also depend significantly on the organizational culture. All the objectives for the BI platform are necessary, but separately not sufficient conditions to achieve faster and more efficient translation. The implementation of the strategy supporting science with technology has to combine and balance the identified factors.

**4. Implementation**

At this strategic level of design, we exemplify an application with three levels for the BI platform in a CTS Center: Business Architecture, Functional Architecture, and Technological Architecture. The architecture offered here harmonizes the BI infrastructure objectives with the organizational objectives identified earlier.

The business architecture defines processes and activities that are central and have a direct impact on translation, as well as other activities that support the key processes. We assert that core processes of a CTS Center are training and mentoring of translational scientists, optimization of the use of resources for translational research, support investigators in study design, analysis, ethics and good practice, provide communication services for stakeholders, and engage with the community. For these core processes to function well, supporting tasks like recruiting students and scholars with the right profiles, finding funds for translational research, and properly managing financial resources and assets of the CTS Center will be necessary. A high level view of the principal processes of the CTS Center is shown in Figure 3.

![Figure 3. Links between business processes](image)

The construction of the functional viewpoint for the architecture has the purpose of structuring the system into communicating blocks that would enable the services of the BI platform. The elements in the functional architecture should support connectivity, optimize data management, define norms and rules for the use of resources, provide tools to control the performance of the system, supply the tools to perform optimally the core processes of the Center, as well as the tools to manage the internal resources.

The technological architecture proposes to balance interoperability and organization of resources. Both approaches can be implemented in a web environment, and are not mutually exclusive. Interoperability federates resources and integrates distributed heterogeneous systems through interfaces; its limitations could be security and reliability of service in large platforms. On the other hand, the semantic web improves the search of information by associating patterns organized in ontologies and infers meaning from the words/phrases searched. This approach not only improves the search of information, but can also be helpful to integrate information from different sources. The limitation of this organization approach is the reduced mass of biological data available in a semantic web context.

**5. Discussion and future research**

In spite of its importance, a gap exists in the study of structures and processes for biomedical innovation [5]. There is also a bias towards behavioral rather than design studies in information systems [32] and a trend to study the optimization of hardware and
software. Those perspectives seem to be operational rather than strategic.

The present study explored the main objectives of the nascent Clinical and Translational Science. We examine at the strategic level how technologies for communication and data management and analysis can be aligned to design strategies that support efficiency and effectiveness to translate basic science into applications for the clinical setting. We have presented one simplified example of how to align the objectives of CTS Center and BI Platform.

Understanding that the BI platform has to be seen not only as a multiple interconnected databases system, but as a psychological, educational, social and technological platform to break the silos, this study could be used to design sound architectures for the emerging CTS Centers in such a way that technology is implemented in a thoughtful and proper manner [33] to achieve the organizational purposes.

6. References


