The Living Human Project: a stair with many steps

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Introduction

The beginning of 2002 was a very fertile period for some of us. The final stage of the VAKHUM project demonstrated that a collaborative effort around data collection could produce an enormous value for biomedical research. The Multimod was up and running since a few months, enough time to become comfortable with the idea of setting up and running large software development projects focused on biomedical applications. The BioNet event produced a lot of excitement around the idea of creating a biomechanics community aimed to overcome the natural fragmentation and the lack of critical mass typical of this research field.

http://www.ulb.ac.be/project/vakhum/

http://www.tecno.ior.it/multimod/

http://www.mk.dmu.ac.uk/bionet/index.htm

All these different inputs slowly shaped into a visionary idea: the creation of the European Biomechanics Lab, organised as Internet-based virtual laboratory to which most biomechanics researchers would participate to some extent. Such an important entity required a comparably important research challenge, which was identified in what we call the *Living Human Project*. The LHP aimed to created a complex combination of large data collections, sophisticated user interfaces, state-of-the-art simulation software environments, and of grid-based distributed computational and storage infrastructures. All these components were necessary to create a generalised model of the human body functional anatomy. The Living human model would let researchers to:

- Access the totality of anatomical information provided by the Visible Human datasets in a format that could be directly used for biomechanics research
- Replace a portion (an organ, a bone, a limb) of the generic model with subject-specific data, with all the tools required to scale the rest of the generic anatomical information to the subject-specific data
- Create collections of multiple instances of any portion of the generic model, with all tools required to use this multiplicity in simulation studies to account for inter-subject variability
- Associate to anatomical data collection of measurements on tissues material properties, movement data, postural data, motor control measurements, etc.
- Use all these data in combination with all the services provided by the simulation environments to create functional simulations, which can be easily customised by using some subject-specific data, or multiple-subject data to run statistical analyses
- Combine these functional simulations with effective user interfaces to build pre-packaged solutions for specific medical problems.

At this point, the vision was quite clear: *To network most European experts of biomechanics, biocomputing and bioinformatics into a virtual laboratory, which would collectively develop the European answer to the visible Human Project: the Living Human Project.*

Rationale of the Living Human Project

The release, some years ago, of the Visible Human (VH) dataset made it possible, for the first time, to access anatomical information without compromises. This produced a significant momentum in many areas but, after a little time, it became clear that, while the dissection approach used in the VH project ensured extreme quality, it also lacked many aspects that other forms of data contain. These

include in vivo data collection, multi-subject, gender, sex, and age variations, lack of connection with functional information, no pathology, etc. To put it simply – he was only a single human, and he is dead. We do not know how he breathed, walked, swallowed, digested – the **VH data totally lacks multiplicity and functionality**.

Many research projects have been carried out in Europe over the last few years, some with the support of the European Commission, to try to circumvent some of these limitations. A basic aspect possessed by the VH project, and lacking in all these other projects, is completeness. The VH project relates ONLY to the normal anatomy of one human subject, and provides ALL the anatomical information for that subject. The other projects had wider objectives, but lacked completeness. Some focused only on pathological data, others only on the lower limb, others again only on the modelling of functional aspects. Because of the lack of the necessary critical mass, none has dared to search for completeness.

The Living Human Project (LHP) will develop a worldwide, distributed repository of anatomo-functional data and of simulation algorithms, fully integrated into a seamless simulation environment and directly accessible by any researcher in the world. This will establish Europe as the leader in the area of human functional modelling, directly challenging the USA Visible Human Project and related initiatives.

The objective is patient-specific bio-numerics (-mechanics, -electromagnetics, etc.) and image-processing (both for pre-processing & visualisation) for the complete human body, with integration of individual systems through hierarchical approaches at the algorithmic level and through middleware operating across distributed systems for Grid computing, using a semantic web to manage the information. The focus of the Grid approach is to provide services to medical or clinical users, removing any need for them to have to handle the details of the computing systems or simulation methods.

The steps we must climb

This very rudimental and somehow naive description of such grand challenge already allowed the identification of some major milestones. A first long list of milestones regards all the information technologies we need to develop and implement:

- Establish the IT infrastructure required to set-up the virtual Laboratory.
- Establish the IT infrastructure required to form, to manage, to make accessible, and continuously update large biomedical data collections.
- Develop a multi-data registration toolkit allowing the averaging of similar data, as well as the merging of subject-specific data with complementary generic or average data.
- Develop a distributed software library to deploy Internet-based multimodal interfaces, customisable toward the application context.
- Develop a scriptable integration middleware providing support for pre-processing the data in the collection (i.e. meshing), support automatic code-specific input formatting, transparent access to commercial and research simulation codes with support for a Application Service Provider model, and automatic code-specific results formatting.
- Creation of a Grid-based computational and storage distributed infrastructure supporting all previously listed services, able to serve efficiently all Europe with an extensible deployment model that makes easy to add new nodes as new computing facilities decide to join the initiative.

At the same time it is necessary that the researchers in biomechanics and related topics are able to achieve these milestones:

- Creating an Internet biomechanics community fully representative of the various branches of the discipline as well as of the various countries that form, or will form in a near future, Europe.
- Organising training and re-training events of biomechanical modelling, the Living Human Project and on the use of the associated technologies.
- Creating awareness on the initiative and establishing communication with the neighbouring disciplines (physiology, anatomy, ergonomy, etc.) and with the natural 'customers': the clinicians, the industries, and the citizens at large.
- Form a sufficiently large (numerous and disparate) data collection.
- Process the anatomical information provided by the Visible Human datasets so to make it directly usable for biomechanics research.
- Extend and complement the Visible Human data collection with functional, pathological and multi-subject data.
- Associate to anatomical data collection of measurements on tissues material properties, movement data, postural data, motor control measurements, etc.
- Develop a systematic organisation of all the possible data (biomechanics and functional anatomy ontology)
- Create functional simulations easily customisable with subject-specific data, or multiple-subject data to run statistical analyses. Combine these functional simulations with effective user interfaces to build pre-packaged solutions for specific medical problems.

How much would it cost?

When we started to make these preliminary plans the message coming from the European Commission was:" the Sixth Framework Program will support only grand, huge projects. Think big, look forward, build a vision". This may partially explain why we aimed so high.

In the first project layout, drafted in the two Expressions of Interests on June 2002 we assumed that all the IT research activities related with the inclusions of functional and of multiple-subject data could be addressed by an Integrated Project, that we entitled the Living Human Project. We roughly estimated a cost of 20 millions Euro over five years to achieve this block of milestones. A second project should create a Network of Excellence called VRLab. This NoE would support the creation and the management of the BEL Community, would build all technological infrastructures for the collaborative work, for the knowledge management, and for the data collection and management. For the VRLab we estimated a cost around the 16 million Euro over six years. As part of the NoE, the 200 and more biomechanics researchers were supposed to express a total value for the so-called joint program action of nearly 50 million Euro. This money would come from other grant agencies, from the industry, from national support to the member research centre, etc.

Thus, in this plan the whole operation would last six years and cost 36 millions Euro of direct EC support, plus another 50 millions Euro of indirect support the partners would bring in as added value by sharing the results of the research activities supported elsewhere. It is important to notice that these figures were in line with the preliminary indications the European Commission was giving in terms of expected size of the projects.

Reality checking

Once the definition of the Sixth Framework Program for Research and Technological Development (FP6) of the European Commission was clearly defined, the idea of finding all the support we need to realise our Grand Challenge from a single project was abandoned.

However, we shall try to submit various proposals, co-ordinated by different institutions, each connected although independent to the overall idea we had. In the follow we shall try to indicate some possibilities in this sense, visible in the first two calls that has been announced by the EC.

General approach foreseen to achieve the objectives

Structure and organisation

The Living Human Project will be co-ordinated by a Core Consortium chaired by the B3C Foundation. This is a research foundation in course of establishment in Bologna by the CINECA Supercomputing Centre and the Istituti Ortopedici Rizzoli, with the collaboration of the University of Bologna, of the regional government of Emilia-Romagna, and of other local economical and industrial institutions. A group of ten staff members from the two founding institutions, with skills ranging from legal matters to grid technology, will cover all general management needs that may originate from the European Commission or from the Consortium itself. In the Fifth Framework Program, CINECA and the Istituti Ortopedici Rizzoli have co-ordinated various projects globally worth various millions of Euro. Many of these projects were presented and successfully managed in collaboration by the two institutions, under the collective name of BioComputing Competence Centre (B3C). The B3C Foundation consolidate and establish this collaboration, formalising it into a separate legal entity, that will operate the LHP Consortium with total autonomy combined to a total support from the two founding institutions.

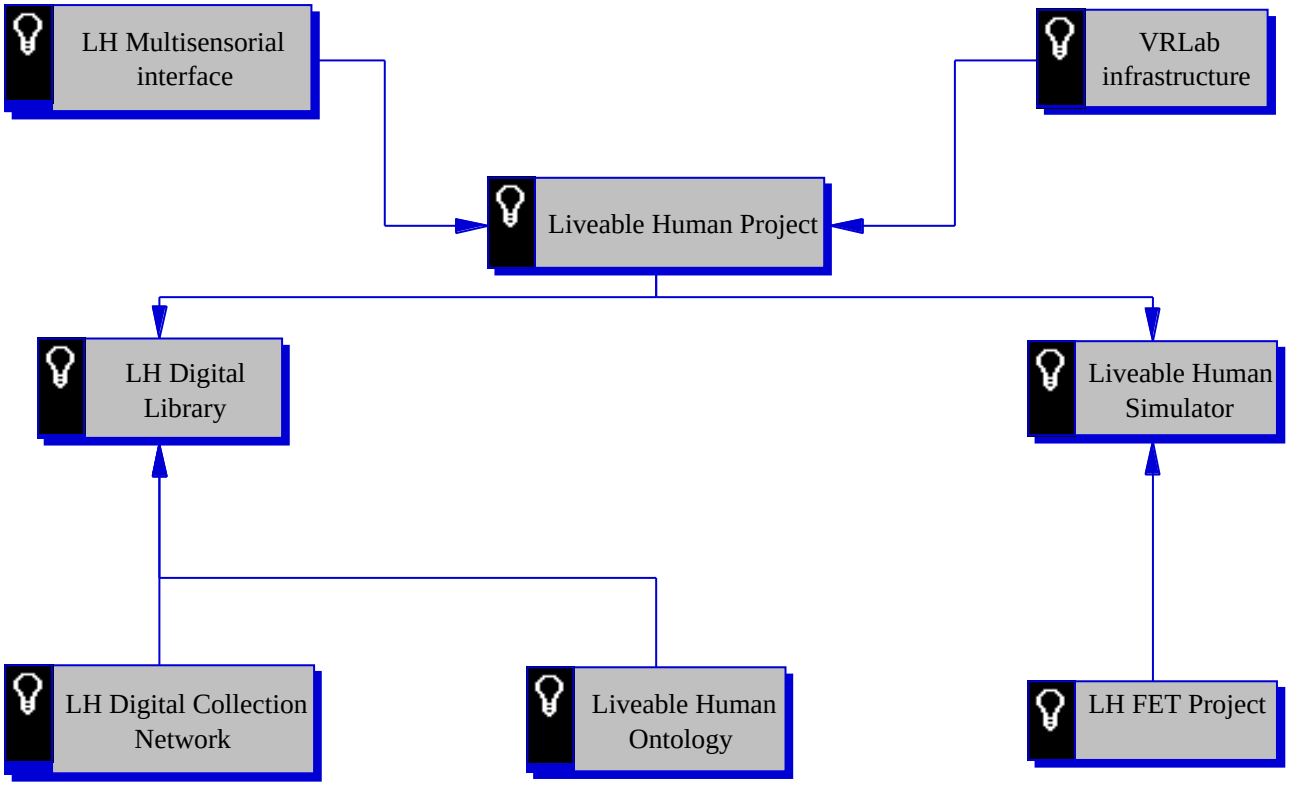
Depending on the general agreement the B3C Foundation may provide a kind of informal management hub for the various sub-projects co-ordinators. Another option that may be considered in a second stage is to create a European Interest Economic Group, giving a single and common legal identity to all co-ordinating organisations.

Architectural overview

Even with the so-called new instruments provided by the sixth Framework Program, the Living Human Project couldn't be fully supported by a single EC grant, or run as single research project. On the contrary we expect to see a certain number of research activities running in parallel. They should be organised to be loosely coupled by highly synergistic, so to minimise the risk and maximise the efficacy of the effort. In the following it is provided an overview of how the final architecture should look like.

The need for multiplicity is addressed by a Digital Library infrastructure able to manage a huge scientific collection of biomechanics and anatomo-functional data. The *Living Human Digital Library* should be a distributed facility, with support for semantic web and knowledge management tools, an effective user interface to the data.

A second component is the Biomechanics European Laboratory, a virtual laboratory born from the BioNet action, around which we are forming the community of experts that will build, maintain and use the Living Human. The BEL Community is already up and running thanks to a voluntary effort of many European scientists. We need to support the creation of the *Living Human digital collection Network* aimed to form and maintain the Living Human Digital Library.



The Functionality is provided by the *Living Human Simulator* a GRID-based biocomputing environment that will support the simulation layer required to merge functional information with anatomical data.

The issue of interfacing effectively the user to such a huge collection of anatomical and functional data may provide an exceptional application domain for the multisensorial interface technologies. The *Living Human Multisensorial interface* will explore this specific research domain and eventually provide innovative ways to access the Living Human collection.

Another parallel research direction is that related to systematic and comprehensive organisation of the domain knowledge into a complete ontology for biomechanics and functional anatomy. The *Living Human Ontology* will provide this structuring framework to the LHP. In a wider approach this research direction may be expanded toward the clinical application, by extending the ontology to support diseases and related anatomical, functional and biomechanics indicators.

Once up and running the Living Human will be a networked organisation of exceptional complexity, involving hundreds and hundreds of researchers, users, data collections, simulation codes, interfaces, and so on. *The VRLab infrastructure* will provide the necessary collaborative software environment that is required to cope with this complexity.

Last, but not least, there are certain aspects of the numerical simulations involving the creation of a Living Human that are still open to dramatic improvements. The *Living Human FET Project* will explore these basic research aspects in terms of future and emerging information technologies.