GLOBAL HEALTH 2013

The Second International Conference on Global Health Challenges

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GLOBAL HEALTH 2013 Editors

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Foreword

The Second International Conference on Global Health Challenges (GLOBAL HEALTH 2013), held between November 17-22, 2013 in Lisbon, Portugal, continued a series of events taking a global perspective on population health, from national to cross-country approaches, multiplatform technologies, from drug design to medicine accessibility; everything under mobile, ubiquitous, and personalized characteristics of new age population.

Recent advances in technology and computational science influenced a large spectrum of branches in approaching population health. Despite significant progress, many challenges exist, including health informatics, cross-country platforms interoperability, system and laws harmonization, protection of health data, practical solutions, accessibility to health services, and many others. Along with technological progress, personalized medicine, ambient assistance and pervasive health complement patient needs. A combination of classical and information-driven approach is developing now, where diagnosis systems, data protection mechanisms, remote assistance and hospital-processes are converging.

We take here the opportunity to warmly thank all the members of the GLOBAL HEALTH 2013 Technical Program Committee, as well as the numerous reviewers. The creation of such a broad and high quality conference program would not have been possible without their involvement. We also kindly thank all the authors who dedicated much of their time and efforts to contribute to GLOBAL HEALTH 2013. We truly believe that, thanks to all these efforts, the final conference program consisted of top quality contributions.

Also, this event could not have been a reality without the support of many individuals, organizations, and sponsors. We are grateful to the members of the GLOBAL HEALTH 2013 organizing committee for their help in handling the logistics and for their work to make this professional meeting a success.

We hope that GLOBAL HEALTH 2013 was a successful international forum for the exchange of ideas and results between academia and industry and for the promotion of progress in the area of global health challenges.

We are convinced that the participants found the event useful and communications very open. We hope that Lisbon, Portugal, provided a pleasant environment during the conference and everyone saved some time to enjoy the charm of the city.

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Abstract—Needs and wishes regarding the interaction with ICT solutions change over time and vary between older adults. They depend on the user's physical and mental capabilities and preferences. In particular usability, accessibility, as well as the freedom of choice concerning the interaction with such systems are the crucial points for acceptability and applicability. The aim of the AALuis project is to offer a practical solution for adapting user interfaces and services to changing needs and wishes of older adults in a flexible way by providing various devices and I/O modalities. The paper describes the approach for the integration of an avatar into the generated user interfaces. The user interfaces aim to provide consistent look and feel for different services to interact using the user's preferred modality. In the first development cycle, the focus was on covering the whole transformation process from abstract task descriptions to renderable UIs to be displayed on various I/O devices. First evaluations in a lab setting have been performed to detect usability issues. The participants gave very positive feedback about the identical layout of the application on different I/O devices, but nevertheless some usability issues have been identified. Solutions to tackle these issues are presented in this paper and especially the avatar integration will be a big step towards an increased acceptance of AAL services and their user interfaces.

Keywords—*Ambient Assisted Living, multimodal user interfaces, avatar enriched user interfaces, adaptability*

I. Introduction

Older adults benefit from information and communication technology solutions and services in the Ambient Assisted Living (AAL) domain. Needs and wishes regarding the interaction with ICT solutions change over time and vary between older adults. They depend on the user's physical and mental capabilities and preferences. Many currently available user interfaces (UIs) for ICT solutions for older adults often do not take these factors into account. And that is problematic, since the user interface has to be considered critical to the success or failure of an ICT product or service [1]. In particular usability, accessibility, as well as the freedom of choice concerning the interaction with such systems are the crucial points for acceptability and applicability. Furthermore, the benefit of such systems for the user him- or herself, for the society and also for other stakeholders depends on these issues [2]. Coherence (i.e., a seamless control of different services and appliances within the user interface), task orientation (i.e., the user interface should allow to start functionalities but not expose how it will be achieved), scalability (i.e., the possibility to reduce

and/or expand the functionality of the user interface) and accessibility (i.e., accessible for a wide range of users) are important features when talking about user interfaces [3].

The aim of the AALuis project [4] is to offer a practical solution for the adaptation of user interfaces and services to changing needs and wishes of older adults in a flexible way by providing user interfaces for various devices and with multiple, possible I/O modalities. These objectives are based on the following three major challenges to improve the way older adults interact with AAL services: (1) Older adults are a very heterogeneous target group. A change of capabilities and needs over time is normal and typical within the process of aging. (2) Exchangeability, flexibility and usability of user interfaces and their standardized integration are of uttermost importance. (3) Freedom of choice regarding the user interface helps with an assisted living lifestyle approach and avoidance of care-stigmatized services are crucial challenges for scalable services.

The generated user interfaces are intuitive and follow recent market trends as the focus is on multi-touch tables, portable devices and smart-TV based solutions. The rendered interfaces offer new intuitive ways of interaction and avatar interfaces simulating a "face to face" communication. Using an avatar as a virtual presenter of information creates additional value, since the addition of a visual display to verbal information can increase the intelligibility and enhance the robustness of the information transmission [5] as known from natural speech [6]. The paper describes the approach for the integration of the avatar into the generated user interfaces, which aim to provide consistent look and feel for different services with the possibility for interactions using the user's preferred modality.

The paper is structured in the following way. After the introduction (Section I) and a brief description of the state of the art in (semi-)automatic user interface generation (Section II), an overview over the used methodologies and approaches is given (Section III). Thereafter, some intermediate results (Section IV) and an outlook for improvements (Section V) are presented. Finally, the presented solution is discussed (Section VI).

II. State of the art

Currently, user interfaces are customized for the device they are implemented for. There are approaches to separate the appearance and control of the user interface from the

device. However, these solutions are focused on the device-independent display of multimedia content and hence are too complex with respect to content delivery and not suitable for the device-independent control of services in the AAL context. To overcome those issues User Interface Description Languages (UIDL) [7] have been invented. Instead of creating an user interface for a specific platform directly, the user interface is modelled in a more abstract format. The model describes the necessary interaction elements of the user interface for all tasks to be carried out in a machine-readable form, which can be used for the (semi-)automatically generation of the renderable user interface.

In recent years, there has been research going on regarding the (semi-)automatic generation of user interfaces. universAAL aims to develop an open platform to ensure technically feasibility and economically viability to conceive, design and deploy innovative AAL services [8]. The approach is to detach the UI bus fully from the service and context bus and to create the user interface using XForms. Another approach is the URC, which is an international standard (ISO/IEC 24752) defining a way to control arbitrary electronic devices or services (i.e., hardware or software) with interoperable, pluggable user interfaces. The UCH [9] realizes the URC standard as a middleware server component providing connection points to existing, non URC compliant entities. Another approach is to use a task model for the creation of the renderable user interface [10] [11], which is the basis for the presented work.

III. METHODOLOGY AND APPROACHES

A. User interface generation and adaptation

In Figure 1, the overall user interface generation and adaptation process is depicted. The generated user interfaces and the services are connected by the intermediate OSGi based AALuis layer, which performs the whole dialog management and transformation process. The middleware layer can either run stand-alone or on top of another OSGi based AAL middleware (e.g., HOMER [12]–[14]).

The services are integrated into the AALuis layer either as an OSGi bundle or as a loosely-coupled web service. To ensure that the service developers just need to take care about their services, but do not need to worry about the final user interface, they have to provide a description of the task flow of the service in concur task tree (CTT) notation [10]. A simple binding file in XML format connects concrete service methods to its corresponding CTT tasks.

The user interface is generated at run-time based on the task flow description. In the transformation process from the CTT to an abstract user interface (AUI) in MariaXML [11] to the renderable user interfaces (RUIs) in HTML5 different information is taken into account: (1) the user preferences, (2) the available devices and their capabilities, (3) service and task context, and (4) environmental context.

A user preference can, for example, be that the user prefers to use the animated talking avatar as an additional output modality to display text information.

B. Generation of the avatar

The avatar generation is carried out on a server with 3D graphics hardware and custom server software components. These components comprise a control server software that
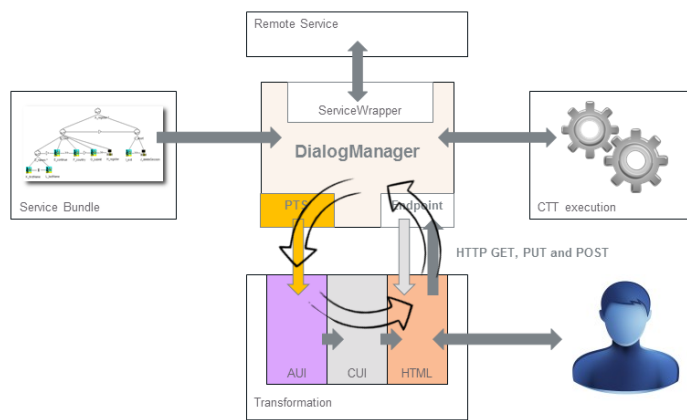
Fig. 1. The AALuis user interface generation process

also contains the logic for animation automation, an audio speech synthesis module, a lip-sync component, a 3D render engine with additional video compression functionality, and a webserver that provides the generated video files. The components communicate via TCP/IP, the control server is queried over the internet via the WebSocket [15] protocol.

A given text is sent to the control software and converted to audio speech by CereProc cServer [16], a commercial test-to-speech synthesizer. As intermediate data of this step a phonetic transcription, i.e., a sequence of phones to be spoken with their durations, is generated. This infromation is used to create control commands for jaw opening, lip opening, lip spreading, and tongue tip raising of the avatar by a numerical articulation model [17] implemented in the lip-sync module. A unique animation script is composed at each request. It layers the speech animation and an adequate sequence of body movements from a large set of animation clips. Words that are prominent in the synthesized audio speech signal are assigned to animation clips that visually emphasize the respective part of the spoken text by hand gestures, head or body movements. The animation script is executed, rendered by a modified 3D computer game engine, and converted by FFmpef [18] into an h.264 video that shows the avatar speaking the given text with speech-accompanying hand gestures and head and body movements.

C. Integration of the avatar

An interface to communicate with the avatar server is directly integrated into the OSGi framework running the AALuis layer. Character and scene settings for the avatar are defined by the service. The text and the settings (e.g., language) are passed on as call parameters and the avatar creation engine returns a reference to the generated and cached video file (Figure 2).

```
VideoObject video =
    zoobeService.getVideoFromText
    (sInputText, sLang, ...)
```

Fig. 2. Code snippet for the avatar creation

Each task can have several input and output parameters. As mentioned in Section III-A, the binding.xml file binds these task parameters to concrete service methods by using a special

AALuis data format (AALuisData). This allows the transport of different data types and is internally realized as a kind of key/value map, which enables the multi-modality support. By the fact that each task is able to serve multiple and different modalities, the transformation process places the current used modality set into the transformation context variable. In Figure 3, one can see a snippet of the context variable representing text and avatar based output.

```
eu.aaluis.context.service.data: {
  "/aaluis/task/AALuisService/Greet": {
    "text/plain":"Welcome to AALuis!",
    "application/x-mpegURL":
    "http://.../cacheManager/0254668.mpeg"
  }
}
```

Fig. 3.   Code snippet for the context variable

Depending on the device and user preference either text/plain and/or the application/x-mpegURL (video) will be rendered. If so, the generated video file is directly embedded in the renderable user interface. The video file is streamed from the server and played when the user interface is displayed. The video file is cached locally and played from the file system, if the same utterance is requested with the same parameters again [2].

IV.   INTERMEDIATE RESULTS

In the first development cycle, the focus was on covering the whole transformation process from abstract task descriptions to renderable user interfaces to be displayed on various I/O devices. In Figure 4, one can see a generated user interface of the first prototype. Usability and the integration of avatars are the main goals of the second development iteration.

First evaluations in a lab setting have been performed to detect usability issues. The participants (two groups - UG1 ($N = 5; 67 \pm 7$ years) and UG2 ($N = 4; 76 \pm 4$ years)) gave positive feedback about the identical layout of the application on different I/O devices, but nevertheless, some usability issues have been identified. These issues covered disappearing navigation possibilities when scrolling down, missing titles on the different screens which led to confusions regarding the actual functionality of the application and the grouping of interaction items (buttons). Concerning the grouping, participants were irritated by the placement of buttons for confirmation/activation (e.g., send message) and navigation jointly at the top of the application.

All participants in user group 1 had general knowledge of technical devices, their own TV, and a mobile phone. All participants in user group 2 were living at home but needed some sort of support. In user group 2, all but one participants had no experience with touch screens and refused to use them or were not able to use them anymore due to health problems.

V.   OUTLOOK

The focus in the second development cycle will be to solve the detected usability issues and on enriching the generated user interfaces. Thus, the specification for the second prototype has been updated based on the evaluation results and the
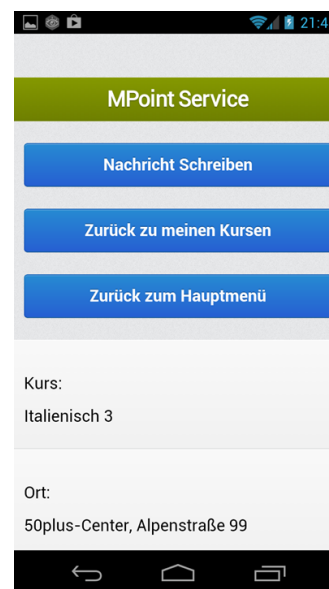
Fig. 4.   Generated UI

integration of images and especially the avatar. As described in Section III-C, the AALuis layer is already capable of avatar integration, but the integration is not yet realized in the transformation process. This will be done in the final prototype. In Figure 5, one can see a sketch for the placement of the avatar as an additional modality for the presentation of information. It is planned to enable the user to start, stop and replay the information presented by the avatar. The figure also illustrates the dual modality by presenting the same information once as text and once as an avatar video as channel for audio-visual speech.

The issue of misleading grouping of interaction items will be tackled by using control types in the abstract user interface which are specified in the MARIA language, namely ACTIVATOR control and NAVIGATOR control. The idea is not to extend the CTT with additional semantic, but just to use the only available interaction task of type CONTROL and to distinguish between NAVIGATION (i.e., to navigate back to the previous rendered user interface), ACTIVATOR (i.e., to execute a POST method on the current rendered user interface) and option controls (i.e., all other controls) in the first transformation step creating the abstract user interface by analyzing the CTT of the service in detail. Option controls are not defined in the MARIA language, thus a grouping mechanism to summarize all controls that will be rendered in the "option" menu will be performed. The title for each presentation task set, which is a group of all enabled tasks at the same time, will be derived from the currently active ACTIVATOR command and be displayed as title for the active screens.

VI.   CONCLUSION AND FUTURE WORK

As mentioned in Section IV, the results of the first evaluations are promising and the overall feedback was positive. Nevertheless there are still some usability and acceptance issues to be solved. Some solutions, which are mainly based on the user feedback, are presented in this paper and especially the avatar integration will be a big step towards an increased acceptance

Fig. 5.   Mock-up with integrated avatar for a tablet

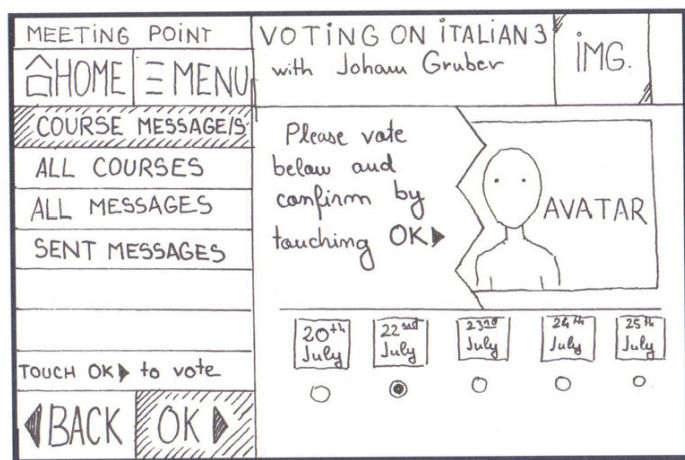of AAL services and their user interfaces. The improvements are all based on the evaluation results, interviews, experiences from other research projects and a former study [19] [20]. Further evaluation tests with older adults, which are planned in the course of the project, will bring deeper insights on acceptability, likeability and usability of avatars within AAL environments.

Generated user interfaces tend in general to be not very user-friendly. AALuis tries to change this using a layered template approach. One of the lessons learned from the first evaluations is that one has to find a good compromise between flexibility and user-friendliness. When dealing with older adults, the usability of the user interface is of uttermost importance. Typically, more user-friendly interfaces are less flexible from the middleware point of view and very flexible user interfaces (being almost completely automatically generated) tend to be less usable. Using the approach of taking user-friendly templates and merging them with accessibility needs and content seems to be promising. However, this approach might be not flexible enough or too complicated and thus has to be evaluated in the future.

The AALuis layer will be released as an open source module and thus can contribute to speed up the development process of AAL services and user interfaces and as a consequence to reduce related costs. Using this strategy, AALuis can be a driving force for the development of new and innovative user interfaces and services for older adults. For this purpose, the acceptance of service developers is of importance; thus, a standardized and relatively easy integration and usage of the AALuis layer in other AAL systems is one of the key objectives.

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High-Performance In-Memory Genome Project:
A Platform for Integrated Real-Time Genome Data Analysis

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Abstract—**A variety of next-generation sequencing technologies reduced costs and improved quality for whole genome sequencing within the last decade. However, interpretation and analysis of generated raw genome data is still a time- and resource-intensive task taking up to weeks. We applied in-memory database technology to form a completely new system architecture that enables processing and real-time analysis of genome data in a single system and reduces time and costs to obtain relevant results, e.g., in the course of personalized medicine.**

Keywords-Genome Data Analysis; Process Integration; In-Memory Database Technology; Personalized Medicine; Next-Generation Sequencing.

I. INTRODUCTION

The Human Genome (HG) project officially launched in 1990 involved thousands of worldwide research institutes and required more than a decade to sequence and decode the full HG [1]. Next-Generation Sequencing (NGS) devices enable processing of whole genome data within hours while reducing costs [2]. NGS is used to support personalized medicine, which aims at treating patients specifically based on individual dispositions, e.g., genetic or environmental factors [3].

The In-Memory Database (IMDB) technology has proven to have major capabilities for analyzing big enterprise and medical data, e.g., to identify relevant patient data and to protect markets from injecting pharmaceutical counterfeits [4], [5].

In this work, we present our findings of applying IMDB technology to enable real-time analysis of genome data in course of our High-performance In-memory Genome (HIG) project. We developed a specific IT platform that combines processing and analyzing of genomic data as a holistic process based on the feedback of researchers and clinicians. Our HIG architecture is designed to run on commodity hardware instead of highly specialized hardware a) to be cost-efficient and b) to make use of existing hardware infrastructures. Fig. 1 depicts the system architecture of our HIG system modeled as block diagram using the Fundamental Modeling Concepts (FMC) [6].
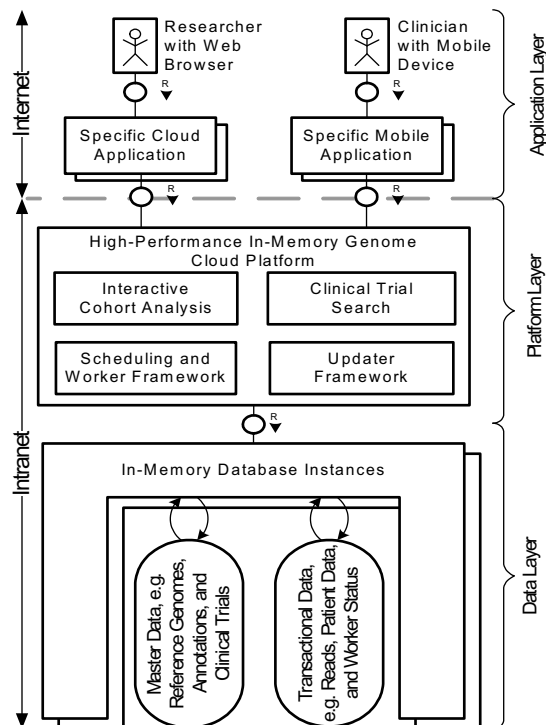
Figure 1. The HIG system architecture consist of application, platform, and data layer. Analysis and processing of data is performed in the platform layer eliminating time-consuming data transfer.

The rest of the paper is structured as follows: In Sect. II, our work is set in context of related work. We introduce selected in-memory technology building blocks in Sect. III and present selected components of our HIG system in Sect. IV. In Sect. V, we share our benchmark results and discuss them in Sect. VI. Our work concludes with an outlook in Sect. VII.

II. RELATED WORK

Fig. 2 provides a comparison of costs for sequencing and main memory modules. Both costs follow a steadily declining trend, which facilitates the increasing use of NGS for whole genome sequencing and IMDB technology for its data analysis. Related work in the
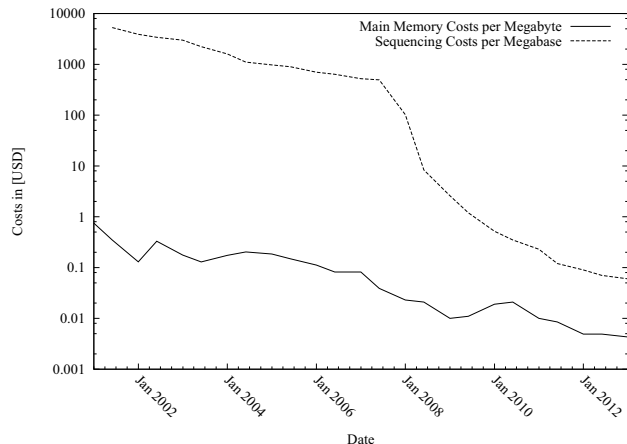
Figure 2. Costs for next-generation sequencing and main memory 2001-2013 adapted from [9], [10].

field of genome data processing has increased in the last years. However, work focusing on implementing end-to-end processes is still rare. Thus, our contribution focuses on supporting integrated processes.

Pabinger et al. evaluated workflow systems and analysis pipeline tools [7]. They realized that existing tools either miss flexibility or the end-user needs additional know-how to install them. We address this by introducing a combined system for modeling and execution of individual pipeline configurations without the need for command line scripts as presented in Sect. IV. Furthermore, Pabinger et al. analyzed a variety of variant analysis tools and evaluated their functionality. For web-based tools they see a drawback in the required data preparation before analysis because "[...] files need to be packed, sorted and indexed before they can be used [7]". We address time-consuming data transformation and preparation steps and replace them by native operations directly performed in our incorporated in-memory database as discussed in Sect. VI.

Wandelt et al. have observed a trend towards more and more cloud-based NGS data management solutions [8, Sect. 4.3]. They identified the efficient mapping of workflow tasks in distributed computing environments and the adjustment of a given workflow to a dynamic environment as open issues. Our work contributes by providing a system architecture that combines processing and analyzing of genome data within a single system. Firstly, the worker framework developed in Python enables integration of computing resources across platform and Operating System (OS) borders. Secondly, the scheduler adjusts the execution of a given workflow, e.g., concrete pipeline process steps. It enables processing of multiple tasks in parallel, e.g., simultaneous users or multiple departments as described in Sect. IV.

III. In-memory Technology Building Blocks

We refer to IMDB technology as a toolbox of IT artifacts to enable processing of enterprise data in real-time in the main memory of server systems [11]. The combination of IMDB database technology and analysis of genome data is driven by the declining cost trends as described in Sect. II. In the following, we outline selected building blocks of the IMDB technology and their relevance for real-time analysis of genomic data.

A. Insert-only

Insert-only is a data management approach that stores data changes as new entries. In contrast to traditional databases destructive update or delete operations do not destroy the original data in an Insert-only table [12, Sect. 7.1]. Instead the data are invalidated, thus keeping complete history of value changes and the latest value for a certain attribute accessible [11]. This approach complies with legal regulations to permanently store clinical data and enables the tracing of decisions within the treatment process, e.g., to retrospectively perform analysis when certain treatments were initiated.

B. Lightweight Compression

Lightweight compression refers to a data storage representation, which consumes less space than its original pendant [11]. A columnar storage layout, as used in IMDBs, supports lightweight compression techniques, such as run-length encoding, dictionary encoding, and difference encoding [13]. Typically, values of a database attribute are within a very small subset of the attribute's domain, e.g., `male` and `female` for the gender type. Lightweight compression maps all unique values to a uniform format, e.g., `male=1` and `female=2`.

C. Partitioning

We distinguish between vertical and horizontal partitioning [14]. The former refers to the arrangement of database columns. It is achieved by splitting columns of one database table in multiple column sets wile each set can be distributed on individual servers [15]. The latter addresses long database tables and their division into smaller chunks of data. Splitting data into equally long horizontal partitions supports parallel search operations and improves scalability [11].

The identification of CpG Islands (CGIs) is a concrete application example. CGIs are known to represent unstable chemical compounds. Its identification requires a full scan of the genome table to find cytosine and guanine bases stored as direct neighbors [16]. Applying a horizontal partition per chromosome for the genome table enables scanning of all chromosomes by individual threads in parallel.

Title	Start Date	End Date	Min Age	Max Age	Rating
Midostaurin (PKC412) for Locally Advanced Rectal Cancer	2011/8	-/-	18/0/0/0/0	0/0/0/0/0	3/4
Chemotherapies Associated With Targeted Therapies on the Resection Rate of Hepatic Metastases	2011/2	2019/2	18/0/0/0/0	0/0/0/0/0	3/4
Dose Finding Study of RAD001 (Everolimus, Afinitor®) in Combination With BEZ235 in Patients With Adv..	2012/1	2014/5	18/0/0/0/0	0/0/0/0/0	3/4
A Phase 2 Study of Panitumumab in Patients With Cetuximab-refractory Metastatic Colorectal Cancer (P..	2012/12	2015/7	18/0/0/0/0	0/0/0/0/0	3/4
Study to Compare Selective Internal Radiation Therapy (SIRT) Versus Sorafenib in Locally Advanced He..	2010/7	2015/7	18/0/0/0/0	0/0/0/0/0	3/3
Vandetanib With Everolimus	2012/5	-/-	0/0/0/0/0	0/0/0/0/0	3/3
Study of 5-Fluorouracil/Leucovorin/Oxaliplatin (FOLFOX) + Bevacizumab Versus 5-Fluorouracil/Leucovor..	2012/7	2017/6	18/0/0/0/0	70/0/0/0/0	3/3

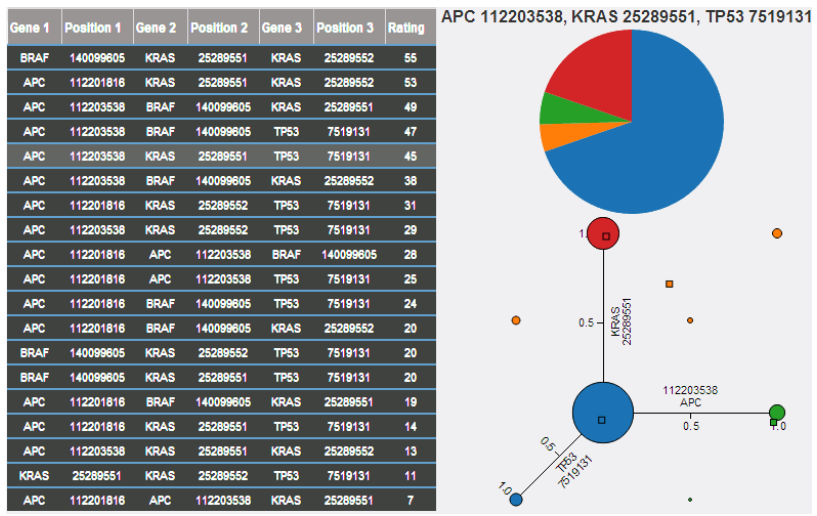| Gene 1	Position 1	Gene 2	Position 2	Gene 3	Position 3	Rating
BRAF	140099605	KRAS	25289551	KRAS	25289552	55
APC	112201816	KRAS	25289551	KRAS	25289552	53
APC	112203538	BRAF	140099605	KRAS	25289551	49
APC	112203538	BRAF	140099605	TP53	7519131	47
APC	112203538	KRAS	25289551	TP53	7519131	45
APC	112203538	BRAF	140099605	KRAS	25289552	38
APC	112201816	KRAS	25289552	TP53	7519131	31
APC	112203538	KRAS	25289552	TP53	7519131	29
APC	112201816	APC	112203538	BRAF	140099605	28
APC	112201816	APC	112203538	TP53	7519131	25
APC	112201816	BRAF	140099605	TP53	7519131	24
APC	112201816	BRAF	140099605	KRAS	25289552	20
BRAF	140099605	KRAS	25289552	TP53	7519131	20
BRAF	140099605	KRAS	25289551	TP53	7519131	20
APC	112201816	BRAF	140099605	KRAS	25289551	19
APC	112201816	KRAS	25289551	TP53	7519131	14
APC	112203538	KRAS	25289551	KRAS	25289552	13
KRAS	25289551	KRAS	25289552	TP53	7519131	11
APC	112201816	APC	112203538	KRAS	25289551	7

Figure 3. Selected HIG cloud applications: The upper Fig. shows the ranked results of our clinical trials search. It includes the patient's history and extracts relevant criteria from trial free-text descriptions with the help of specific rules to identify relevant studies, e.g., clinical trial for advanced rectal cancer started in Aug. 2011. The left Fig. shows the results of an interactive analysis of a cohort of colon carcinoma patients using k-means clustering. It proposes relevant combinations of genomic loci, such as gene KRAS and on chromosome 12 at position 25,289,551, which are present in the majority of cohort members.

IV. ARCHITECTURE

Our HIG system architecture modeled in Fig. 1 combines data from various data sources, such as patient-specific data, genome data, and annotation data within a single system to enable flexibly real-time analysis and combination. In the following, its layers are described in further detail.

A. Application Layer

The application layer consists of special purpose applications to answer medical and research questions. We provide an Application Programming Interface (API) that can be consumed by various kinds of applications, such as web browser applications or mobile applications. Fig. 1 depicts the data exchange via asynchronous Ajax calls and JavaScript Object Notation (JSON) [17], [18]. As a result, performing specific analyses is no longer limited to a specific location, e.g., the desktop computer of a clinician. Instead, all applications can be accessed via device connected to the Internet, e.g., laptop, mobile phone, or tablet computer. Thus, having access to relevant data at any time enhances the userÕs productivity. Selected HIG cloud applications are depicted in Fig. 3, which are described in the following. The end user can access these cloud applications via any Internet browser after registration.

1) Cohort Analysis: The HIG cohort analysis application enables researchers and clinicians to perform interactive clustering on the data stored in the IMDB, e.g., k-means and hierarchical clustering [19, Chap. 13]. Thus, they are able to verify hypotheses by combining patient and genome data in real-time. Therefore, they use patient-specific and genome data loaded into the in-memory database system and perform the interactive cohort analysis as part of the platform layer as depicted in Fig. 1.

2) Clinical Trial Search:: Our HIG clinical trial search assists physicians in finding adequate clinical trials for their patients. It analyses patient data, such as age, gender, preconditions and existing mutations, and matches them with open clinical trials. The analysis is performed on top of more than 30k descriptions of searching clinical trials, which are ranked in real-time while the physician investigates the list of variants in the patient's genome [20].

B. Platform Layer

The platform layer holds the complete process logic and consists of the IMDB system for enabling real-time analysis of genomic data. We developed specific extensions for the IMDB system to support genome data processing and its analysis. In the following, selected extensions and their integration in the IMDB system are described in more detail.

1) Scheduling of Data Processing: We extended the IMDB by a worker framework, which executes tasks

asynchronously, e.g., alignment of chunks of genome data. It consists of a task scheduler instance and a number of workers controlling dedicated computing resources, e.g., individual computing nodes. Workers retrieve tasks and parameters by the scheduler instance and perform specific tasks, such as workbench preparation, task execution, and maintenance of status information. Thus, all workers are connected to the IMDB to store status information about currently executed tasks.

Furthermore, the scheduler supervises the responsiveness of individual compute resources. If a predefined response behavior is no longer guaranteed, e.g., due to an overloaded compute node or a crashed worker process, workers are marked as unresponsive. As a result, work-in-progress tasks of the unresponsive worker are reassigned to a new worker and this worker is scheduled for a restart.

2) Updater Framework: We consider the use of latest international research results as enabler for evidence-based therapy decision [21]. The updater framework is the basis for combining international research results. It periodically checks all registered Internet sources, such as public FTP servers or web sites, for updated and newly added versions of annotations, e.g., database exports as dumps or characteristic file formats, such as CSV, TSV, and VCF. If the online version is newer than the local available version, the new data are automatically downloaded and imported in the IMDB to extend the knowledge base.

The import of new versions of research databases is performed as a background job without affecting the system's operation. We import new data without any data transformations in advance. Thus, they are available for real-time analysis without any delay [22], [23]. For example, the following selected research databases are checked regularly by our updater framework: National Center for Biotechnology Information (NCBI), Sanger's catalogue of somatic mutations in cancer, University of California, Santa Cruz (UCSC) [24], [25], [26].

C. Data Layer

The data layer holds all required data for performing processing and analyzing of genomic data. The data can be distinguished in the two categories: master data, and transactional data [27]. For example, human reference genomes and annotation data are referred to as master data, whereas patient-specific NGS data and Electronic Medical Records (EMR) are referred to as transactional data [28], [29]. Its analysis is the basis for gathering specific insights, e.g., individual genetic dispositions, and for leveraging personalized treatment decision in course of personalized medicine [3].

The actual step of analyzing the genetic data requires answering very specific questions. Thus, the application

TABLE I. CONFIGURATION OF BWA BENCHMARKS.

Experiment	Split Size	Primary Storage
1	1	File System
2	1	In-Memory Database
3	25	File System
4	25	In-Memory Database

layer consists of specific applications to answer these questions. They make use of the platform layer to initialize the data processing.

V. BENCHMARKS

All benchmarks were performed on a computing cluster consisting of 25 identical computing nodes. Each of the nodes was equipped with four Intel Xeon E7-4870 CPUs running at 2.40 GHz clock speed, 30 MB Intel Smart cache[30], interconnected by 6.4 GT/s Quick Path Interconnect (QPI), and 1 TB of main memory capacity. Each CPU consisted of 10 physical cores and 20 threads running a 64-bit instruction set. All computing nodes were equipped with Intel 520 series Solid State Drives (SSDs) of 480 GB capacity combined using a hardware raid for local file operations [31]. The average throughput rate of the local SSDs was measured with 7.6 GB/s cached reads and 1.4 GB/s buffered disk reads. All nodes were interconnected via a Network File System (NFS) using dedicated 10 Gb/s Ethernet links and switches to share data between nodes.

Instead of using generated test data, we only used real NGS data, i.e. FASTQ files, from the 1,000 genome project for individual measurements [32]. We used the FASTQ file of patient HG00251 for our benchmarks. It consumed 160 GB of disk space, consists of approx. 63 Gbp, approx. 695 M reads with 91 bp individual read length forming approx. 20x coverage.

The aim of all conducted benchmarks was to minimize the overall execution time for a single GDPP run, i.e. to use the maximum available computing power to achieve best parallelization. In the following, we share insights about our benchmarks performed on our HIG system.

A. Performance Key Indicators

We investigated the following impact factors to controlling the overall pipeline execution time:

1) **Integration:** We implemented GDPPs based on existing alignment and variant calling tools in our system architecture without any modification of the established tools,
2) **Adaption:** We adapted existing GDPPs to use the in-memory database as primary storage for data processing, and
3) **Optimization:** We optimized the number of involved distributed computing nodes (`split size`).
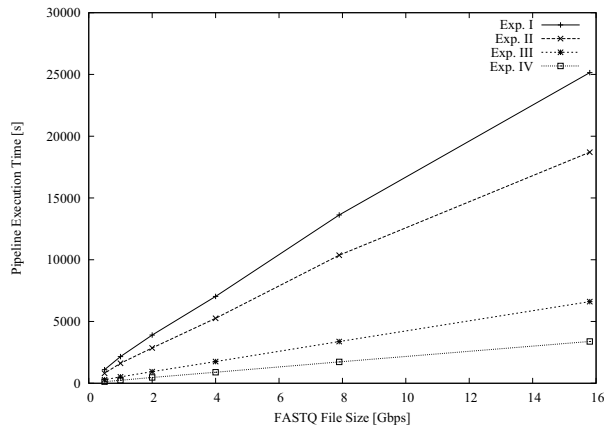
Figure 4. Comparison of benchmark results. Exp. 2 shows relative improvements of 24-27 % on single computing node compared to Exp. 1. Exp. 3 and 4 show relative improvements up 76 % and 89 % resp. on 25 computing nodes compared to Exp. 1 (Exp. = Experiment).

TABLE II. COMPARISON OF OVERALL PIPELINE EXECUTION TIMES IN HIG. T_X=EXECUTION TIME FOR EXP. X, A_X=RELATIVE ADVANCE OF EXECUTION TIME FOR EXP. X COMPARED TO EXP. 1 AS $A_X = \frac{T_1 - T_X}{T_1}$.

Size [Gbp]	0.5	1.0	2.0	4.0	7.9	15.8
$t_1[s]$	1,100	2,159	3,900	7,029	13,626	25,147
$t_2[s]$	808	1,622	2,860	5,259	10,364	18,707
$t_3[s]$	283	520	943	1,761	3,377	6,609
$t_4[s]$	130	245	470	893	1,733	3,387
$A_2[\%]$	27	25	27	25	24	26
$A_3[\%]$	74	76	76	75	75	74
$A_4[\%]$	88	89	88	87	87	87

B. Results

Our benchmarks were performed on a GDPP integrating Burrows Wheeler Aligner (BWA) version 0.6.2 as selected alignment algorithm [33]. We designed our benchmarks to compare the impact of the incorporated storage and the level of parallelization on the overall execution time as outlined in Tab. I.

Exp. 1 and 2 used a file system as primary storage while an IMDB was used for Exp. 2 and 4. Exp. 1 and 2 were executed on a single computing node, while Exp. 3 and 4 were executed on 25 computing nodes to evaluate the impact of a fully parallelized execution environment.

The overall pipeline execution for varying FASTQ file sizes was measured. BWA was configured to use 80 threads, which relates to the maximum available hardware resources of our benchmark systems.

Exp. 1 and 2 describe the overall pipeline execution time on a single computing node as shown in Tab. II. It depicts that the use of the in-memory database as primary storage for intermediate results is beneficial for all selected file sizes. This pipeline optimization results in a reduction of runtime by at least 25 percent in average.

Exp. 3 and 4 as shown in Tab. II document the

impact of the parameter `split size`, i.e. the number of distributed computing nodes used for parallel execution. Parallel execution of selected pipeline steps reduces the overall execution time by at least 74 percent in average for BWA. Additional improvement can be achieved by using the in-memory database as primary storage. Thus, the overall execution time can by reduced by at least 87 percent in average.

VI. EVALUATION AND DISCUSSION

Our conducted benchmarks verify two hypotheses. Firstly, the usage of the IMDB as primary storage system improves the overall execution time of established alignment algorithms, such as BWA, integrated in our HIG system as depicted in Fig. 4. Secondly, our HIG system supports the parallel execution of intermediate process steps across multiple computing nodes, which results in an additional performance improvement compared to the execution on a single computing node.

We observed the best relative improvement with the adapted pipeline using the IMDB as primary data storage with at least 74 percent on single computing node and up to 89 percent on 25 computing nodes. It shows that the overall pipeline execution time correlates to the number of base pairs contained in the FASTQ file in a very constant and linear way. However, the improvement of using 25 nodes is still below our expectation of a factor 25 since we also use traditional tools in the GDPP, which partially operate in a single threaded way.

The scaling factors for the overall execution time varies between 1.80 and 1.96 across all experiments and file sizes. This indicates a very constant and predictable system behavior of our HIG system for varying input file size. It helps us to predict execution times and helps to supervise the correct system functionality, e.g., to detect broken computing resource as outlined in Sect. IV.

Furthermore, our results stress the benefits of using an IMDB for operating on intermediate results of the pipeline execution. The pipeline optimized for the IMDB no longer uses individual tools operating on files for specific process steps, such as sorting, merging, and indexing. In contrast, these operations are directly performed as an integral operation of the IMDB without the need to create intermediate files in the file system any longer. We integrated existing alignment and variant calling tools into our HIG architecture without modifying their code. Thus, the speed-up documented in our benchmarks is moderate and mainly achieved by replacing selected file-based by optimized in-memory database operations.

VII. CONCLUSION AND OUTLOOK

In our contribution, we shared details about our HIG system enabling genome data processing on an IMDB. We outlined the applicability of this technology for

processing of genome data to enable real-time analysis of genome data. Furthermore, we shared insights in specific design decision for our IT architecture, such as scheduler and updater framework. The presented benchmark results proved that our HIG system improves overall pipeline execution time by at least one fourth on a single computing node and up to 89 percent involving our computing cluster with 25 nodes. The performance improvements are achieved by substituting selected disk-based operations, such as sorting, merging, and indexing, by native in-memory database operations.

Our future research work focuses on optimizing alignment and variant calling algorithms executing them directly within the IMDB. As a result, the amount of media breaks and incorporated data transfers would be reduced further.

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Cognitive Stimulation, Maintenance and Rehabilitation

Designing the user interface, research and practical results

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Abstract — **Significant demographic changes in developed countries in recent decades have reflected the worrying trend of an ageing population, including the Portuguese population. In light of this scenario, there is an urgent need to create solutions that help to mitigate the collateral effects of ageing. This paper describes the development of an occupational health component aimed at enabling technicians and specialists to define and personalize therapeutic intervention programs for cognitive rehabilitation and maintenance, specific to various types of cognitive disabilities. The occupational health component of Mind.Care is being developed under the TICE.Healthy project, whose main objective is to provide a range of activities for the cognitive stimulation, maintenance, monitoring and rehabilitation of the cognitive functions – memory, attention, language, executive functions, visual and special abilities – suited to different user profiles. In addition to the scientific framework, there is an emphasis on conceptual and development decisions, illustrated by the various stages of functional specification, with a definition of usability and accessibility guidelines, design and implementation. The work has a strong scientific foundation and has been developed with great care in terms of design and technological issues, with a view to making a significant contribution to healthy ageing.**

Keywords-mind.care; cognitive stimulation; cognitive maintenance; cognitive rehabilitation; user centered design

I. INTRODUCTION

Cognitive impairment and dementia are the major health issues among older people. By consensus, age has been considered as a major risk factor for developing dementia, including Alzheimer's disease (AD) [1 – 4] and, more recently, Mild Cognitive Impairment (MCI) [5].

It is estimated that the number of patients with dementia will double every 20 years, approaching the 42 million mark in 2020 and reaching 81 million by 2040, in the absence of effective treatments or preventive strategies [6]. In Portugal, it is estimated that there are approximately 153.000 patients with dementia [7]. The serious impact of the aging population and specifically of the AD in health-care systems worldwide [8, 9] and the dramatic projections for the coming years [6, 10], also expected in the Portuguese population, stress the need for new effective strategies able to address with this scenario.

Besides a brief description of the Mind.Care's occupational health component and the importance of cognitive stimulation, this paper describes the user-centered design methodology adopted in the project development and all the constraints of the target users. There is an emphasis on conceptual and development decisions, illustrated by the various stages of functional specification, with a definition of usability and accessibility guidelines, design and implementation. After describing a typical cognitive activity experience, Mind.Care's project is also presented as an integrated project.

A. *The importance of cognitive stimulation*

With aging, the ability to receive, process and remember information tends to deteriorate. Healthy aging and stimulation of the various cognitive skills is clearly a way to mitigate this situation. Numerous studies clearly prove that older people, with a lifestyle which includes intensive cognitive stimulation, have a better global cognitive functioning, a greater ability to think and tend to delay the onset of cognitive decline [11, 12].

Frequent cognitive activity protects and slows cognitive decline because it stimulates different parts of the brain involved in memory and information processing, making them more efficient and resilient. The resultant increase in the number of brain cells and the connections between them contribute to a greater cognitive reserve and reduces the risk of dementia.

Several studies have confirmed the increased risk for the development of dementia in patients with MCI. Currently, recent studies reporting incidence rates of MCI close to 6.4% [13] and prevalence rates about 16% [14]. In this context, the MCI phase is the ideal target for implementation of stimulating activities and cognitive training, allowing early intervention in times of incipient cognitive decline and reducing its severity.

B. Our solution

The component for occupational health Mind.Care is focused on stimulation, maintenance and cognitive rehabilitation of seniors. This component will provide a range of brain training activities that stimulates several cognitive functions, including: memory, attention, language, executive functions and visuospatial abilities.

Following any brain damage, cognitive disorders, in particular memory deficits, are common in patients and have a major impact on their lives and those of their caregivers.

Given the small number of platforms targeted at cognitive training, specifically for the Portuguese population, it is a matter of some urgency to create and encourage those activities that can best help experts in the field of neuroscience to stimulate, rehabilitate and maintain the various cognitive functions of their patients.

The component for occupational health Mind.Care will provide a set of services that will:

- Allow health professionals and experts to define and customize the therapeutic intervention programs for cognitive rehabilitation or maintenance, specific to various types of cognitive disorders, by selecting multiple activities that meet the needs and difficulties of each patient;
- The activities suited to different needs of stimulation/maintenance/rehabilitation of various neurodegenerative diseases, which can stimulate various cognitive functions including memory, attention, language, executive functions, spatial perception;
- Enable health professionals and experts to monitor and measure the performance and clinical evolution of each patient;
- Allow any healthy senior the access to stimulating activities and cognitive training.

The early stage of preliminary studies first surveyed the state of the art, focusing on identifying and analyzing a range of comprehensive brain training and diagnostic support, maintenance and monitoring platforms for patients with various types of neurodegenerative pathologies. It subsequently looked at the important aspects of usability and accessibility in the context of cognitive impairment and appropriate technologies to implement the activities to be developed.

After these studies, we went on to identify and define the various user profiles, associated services and the characterization of the activities to be developed.

The practical validation of all such activities will be done through a pilot study with clinical and control groups, and should be able to assess not only the preventive capacity and improvement, but the acceptance by and interaction of users. In short, we intend to find out if the activities are appropriate to the clinical profiles and really appraise what is wanted for a subsequent clinical validation.

II. USER CENTERED DESIGN

To create a system like the one presented in this paper, it is crucial to ensure the end result is easy to use, but it is also necessary for it to meet the needs of all the actors involved.

Therefore, from concept generation to testing, via the entire implementation phase, a user-centered methodology was adopted.

"*User experience*" was also one of the key concepts that informed the development of this system and carried significant weight, seeing as this is a system aimed at healthy seniors, but also users with a clinical profile, within the remit of cognitive impairments.

In brief, this system comprises a clear understanding of its target users, it communicates its scope and objectives in an unambiguous and straightforward manner, thus embodying something useful, easy to use and appealing.

A. User profiles

These activities, their degrees of difficulty and progress metrics have been defined according to the different user profiles. Each user profile is intended for individuals with different levels of cognitive impairment in the continuum between the cognitive changes due to normal aging (*Healthy Profile*) and clinical conditions of mild cognitive impairment (*Light Profile*).

The *Healthy Profile* is applicable to all healthy adults and seniors who wish to enhance their cognitive skills through cognitive training.

The *Light Profile* will include all adults and seniors who have mild cognitive impairment, clinically significant, non-normal to the aging process but insufficient for clinical diagnosis of dementia. This profile is designed for all patients with a clinical decline beyond that expected for age and education of the individual and which may precede various clinical conditions, particularly but not exclusively dementia diagnosis.

Each activity will always be presented with a level of increasing difficulty (variable in each of the profiles) and accompanied by simple guidelines to follow.

B. Designing for older adults

When creating systems for older adults it is essential to consider the changes that occur naturally with ageing, in particular regarding mobility, hand-eye coordination and motor coordination, the senses, such as hearing and vision, or cognitive abilities, such as short-term memory [15, 16].

In terms of vision, this includes difficulty in distinguishing certain colors, adapting to changes in lighting levels, and a growing difficulty in concentrating, especially when reading, since the ability to focus decreases and so the ability to see close-up becomes increasingly difficult [15].

Changes in the musculoskeletal system can also very often restrict people's functional ability and even prevent them from performing basic daily activities unaided. As mentioned in [17], the review of clinical studies carried out in Portugal up to 2002, which quantified the prevalence of rheumatic diseases and their economic and social impact, showed that rheumatic diseases were the most prevalent chronic pathology (accounting for 28% to 37% of chronic

illnesses). This makes them the foremost reason for Portuguese people attending primary healthcare facilities: 20% of general practice appointments are prompted by rheumatic diseases.

These changes are important and should be taken into consideration because they may make it hard for some people to use certain devices such as the computer mouse or keyboard.

Understanding the main characteristics and limitations of healthy senior users was extremely important. While creating the system, these factors influenced the definition of usability guidelines and clearly interfered in areas like human-computer interaction, browsing (user experience design), information design, functional model, graphic interface (user interface design) and definition of content.

C. Designing for people with cognitive disabilities

Cognitive limitations cover a vast field, with specific needs that depend on the type of pathology. They give rise to a wide range of characteristics/limitations that need to be considered when creating systems for users with this clinical profile. Nevertheless, it is possible to identify the abilities that are most affected by limitations of this type and the main difficulties experienced by individuals with cognitive disabilities [18]. Among them are perception and processing, memory, ability to solve problems, and attention.

We therefore face several challenges:

- Individuals with learning difficulties usually have serious limitations in terms of interpreting and understanding texts, numbers, spoken instructions and difficulty with spatial orientation [19].
- Individuals with a brain injury or cognitive impairment often need more time to interpret and respond to online stimuli [20].
- Individuals with memory problems find it harder to deal with sequential operations or understand and retain information inserted into a complex interface and presented in a haphazard manner [21].
- Individuals with low reflexes or memory and perception problems have a greater difficulty in using buttons on a computer mouse for separate actions [21].

III. CONCEPT

During the whole process of conceiving (functional design, graphic design and technical development) special specificities were taken into account [22]. Design was focused on following concepts - User Centred Design (UCD), User Experience (UX) and User Interface Design (UID) - and a special attention was given to high level of usability.

The most relevant tasks considered during Mind.Care´s concept process were:

- During the specification phase, functional mockups were designed with the main objective to ensure that all users will be able to simply and accurately manipulate all interface and navigation components of cognitive training activities.
- General usability guidelines were also defined to ensure that all interface components were designed so that users of all ages can understand them, even if they have vision impairment or cognitive disabilities.
- A library of simple icons, easy to understand and appropriate to all main actions, was created.
- To guarantee good readability and increase legibility, different typefaces were tested to select those fonts which were best suited to complement the icons and ensure clarity.
- A contrast analyzer was also used to check the combination of colors, based on the requirements of the Web Content Accessibility Guidelines (WCAG) 2.0, ensuring there is sufficient contrast between foreground and background elements.

Following analyses and development of these requirements, the base interface was designed for use in all activities.

A. User interface

Much of the literature related to senior users and the internet eventually suggest guidelines that are reflected in best practice in the creation of systems for any age group and any type of user, from the consistency of browsing, to how to write clearly or how to handle the whole graphical interface [23].

Overall, the approach to reconciling to the full the requirements of the different target audiences of the system to be developed concerns the adoption, where possible, of the principles of universal design. Thus, the end result is meant to deliver a system that is suitable for both healthy senior users and users with cognitive limitations.

The authors of the principles of universal design specify seven principles to consider during the design process and as a way to evaluate products, systems or environments already created - Equitable use, Flexibility in use - Simple and intuitive, Perceptible information, Tolerance for error, Low physical effort, Size and space for approach and use [24].
The main guidelines identified and considered to put into practice the principles mentioned above were:

- To create an interface as intuitive and simple to use as possible, with information organized and structured in a clear, logical and relevant manner for those who use it, but attractive to atract the attention of various types of user.
- To create a system that, whenever possible, is flexible and adaptable to aptitude of each user;
- To integrate a system for speech recognition that could be an alternative mode of interaction through commands made by you.
- To clearly provide multimodal sequential instructions that would help with performing complex operations.
- To create a browsing structure consistent throughout the system, maintaining the coherence

of elements that perform the same type of functions, using graphics and easily recognizable icons, which should aid understanding and browsing.

- To use familiar pictures and graphics that are easy to understand and retain, alongside a simple, clear language – short, concise sentences.
- To ensure maximum contrast between the interface elements (content / background).
- Within the navigation menus and buttons that trigger actions, to associate (whenever possible) graphics with words in order to facilitate understanding.
- To use graphic elements that efficiently communicate what was intended and that are as simple as possible.
- To use sound to supplement the information presented.
- To use sounds that reflect the interaction of the user interface elements, and catch the attention of the user.
- To limit the number of options to avoid overwhelming the level of understanding and retention of information.
- Where justified, to allow the user to cancel accidental and wrong interactions.
- To avoid simultaneous tasks and keep to a minimum the number of steps required for the interaction.
- To increase the size of the clickable areas so as to facilitate interaction for people with impaired vision or motor coordination.
- To allow sufficient time for the user to interact with the content.

IV. PROTOTYPE

Each cognitive activity has an introduction (e.g., name of the activity, cognitive domains to stimulate, the level at which the user is located), a brief presentation, the proposed objectives and is accompanied by a demonstration (Fig. 1).

Before beginning an activity, the user has access to the different levels of difficulty available, and can refer to the parameters that vary between them (Fig. 1).

In performing each activity, the user receives instructions on how to proceed (Fig. 1).

At the end of the activity, the user always has access to an evaluation of performance and may consult, when appropriate; responses are marked as correct or incorrect, when applicable (Fig. 1).

A. The cognitive activity "Spot the differences"

In this activity [22], two seemingly identical pictures are presented simultaneously. The participant must identify and flag the differences between the two images. As the level of difficulty increases, the number of differences increase and these differences become less and less apparent. Additionally, at lower levels of difficulty, images specifically designed for the activity are used, while higher levels of difficulty use images from real situations.

This activity involves predominantly attentional capacities. The task of finding differences between two seemingly identical images implies a flexible mediation between concentration, inhibition of distraction and the ability to shift consciousness from one focus to another. Through the attentional cognitive processes, there is a selection of relevant stimuli to perform a comparative analysis of the details of the figures, while irrelevant information is inhibited, i.e., the various aspects of the images that are not different.
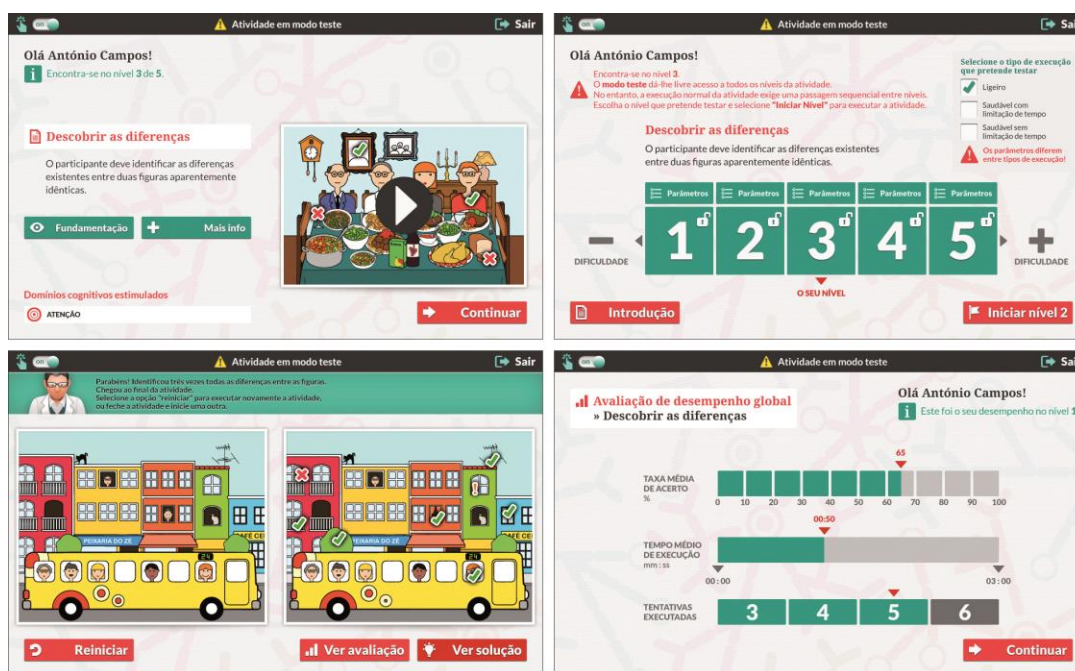

Figure 1. Mind.Care - The cognitive activity "Spot the differences"

V. MIND.CARE'S PROJECT

The Project, Product or Service (PPS) named Mind.Care is framed in the mobilizing project TICE.Healthy. This project, according to the mission and goals of the main TICE.PT, is aimed at enhancing the contribution of Portuguese companies and organizations in global markets of the strategic area "Health and Quality of Life".

TICE.Healthy, where MediaPrimer (www.mediaprimer.pt) is the leading partner, represents a collaborative initiative of Portuguese companies and entities of the Scientific and Technological Sector for the development and marketing of innovative products in the field of e-health.

The Mind.Care project aims to provide services, equipment and aids for the relatives, caregivers and healthcare professionals of persons affected by dementia diseases. The goal is to improve the quality of life and well-being of people suffering from Alzheimer's and Parkinson's diseases, while at the same time significantly reducing the cost of treatment and follow-up of these patients. All is intended to be achieved through the use of a system supported by internet and mobile communications technology.

VI. CONCLUSION AND FUTURE WORK

Mind.Care, is being developed with professional input at all levels. The Centre for Neuroscience and Cell Biology (CNC) of the University of Coimbra provides the scientific support and MediaPrimer is responsible for the design and implementation of the occupational health component, in its various aspects, from graphic design to technological solutions.

Currently, clinical and functional validations of the cognitive activities of the Occupational Health component are being planned. In the near future, the validation of the activities will be initiated expecting to:

- Be carried out through a pilot study with clinical groups who underwent a comprehensive neuropsychological assessment and complete clinical evaluation, either at the beginning or at the end of the validation period;
- Perform psychometric and clinical validation studies, in order to confirm that the several activities of cognitive training are appropriated and useful both user profiles;
- Evaluate the improvement capacity;
- Evaluate the preventive capacity through a longitudinal study;
- Evaluate the acceptance and interaction from users.

After completing the analysis of the data from the clinical observation, technical observation and personal experience of all the actors involved in the pilot study, the next step will be to correct and improve the usability and functionality. These will look at all the difficulties expressed and the improvements suggested that are deemed relevant and essential.

The number of levels for each activity, the respective parameters and degree of difficulty, the type of content and its characteristics, the execution time, and functions available will be reviewed according to the findings of the pilot study.

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Effect of GSM Electromagnetic Waves on the Activity, Morphology, and Structure of Skeletal Muscles

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Abstract—**The use of cellular technology is overwhelming our lives these days. GSM waves - the basis of cellular technology - are high frequency, high energy electromagnetic waves that may pause as a threat to man. The current work studies the effect of such waves on two types of skeletal muscles, the slow and fast twitching muscles. The activity, morphology, and structure of the affected muscles are studied and analyzed against control. Our results shows that in both muscles, there were changes in the distribution of muscles proteins and in the percentage of MHC isoforms suggesting that the GSM antenna relay affects the plasticity of skeletal muscle fiber by transforming slow type to faster one.**

Keywords-GSM electromagnetic waves; skeletal muscles; proteins content; testosterone level; MHC isoforms.

I. INTRODUCTION

Striated muscle myofibrils are composed of repeating units called sarcomeres that are arranged in series. Sarcomeres in turn are composed of contractile filaments termed myofilaments that are of two major types, actin (thin filament) and myosin (thick filament), which interact together to generate force and contraction. These myofilaments are large polymers of noncovalently associated contractile proteins, actin and myosin, that comprise 70% of myofibrillar proteins in skeletal muscles [1]. The isomers of Myosin Heavy Chains (MHC) are often used to distinguish the types of skeletal muscle fibers: slow-twitch – or type I – muscle fibers, where MHC I isoform is abundantly expressed; and fast-twitch – or type II – muscle fibers (types IIa, IIb, and IId/x), where MHC IIa, IIb, IIx/d predominate respectively [2-4]. Slow-twitch fibers are adapted for continuous activity, and they are rich in myoglobin and oxidative enzymes. A typical example is the soleus muscle. Fast-twitch fibers are adapted for rapid activity, and they produce energy through glycolytic metabolism. A typical example is the *extensor digitorum longus* (*edl*) muscle [5].

A remarkable characteristic of striated muscles is plasticity. This term refers to the ability of these muscles to remodel and thus change their contractile and metabolic makeup, and – hence – their type from slow to fast, or vice versa, in response to specific environmental challenges, such as exercise, temperature, or gravitational loading, or internal challenges such as nutritional conditions as well as neuronal, mechanical, metabolic or hormonal stimuli [6]. This may be attributed to a reversible change in the muscle gene expression that leads to reversible structural and functional modifications [7].

One of the important challenges that have developed in the last decade and is thought to have an effect on health is the population exposure to electromagnetic waves, particularly the Global System of Mobile communication signals (GSM) signals. These signals are emitted from diverse sources particularly from cell phones and base station antennas. Also, they may come from industrial processes where workers in broadcasting, transport, and communication industries are highly exposed. They are also emitted from medical devices like electrosurgical devices and diagnosis equipment. Thus, concerns from the risk of GSM signals on health arise from long term exposure as well as from the cumulative effect of these waves. The major mechanism by which such waves can induce an effect on biological systems is the thermal mechanism by which the Electromagnetic Field (EMF) at high intensities can increase the tissue or body temperatures above the normal

value. Non-thermal mechanisms are under wide investigation in recent studies [8-11].

Few studies have investigated the effect of electromagnetic waves on skeletal muscles. In fact, Radicheva *et al.* in 2002 has shown that a 2.45 GHz microwave field could possess a stimulating effect on muscle fiber activity, which is in part due to its specific non-thermal properties [12]. Moreover, our previous study has shown that one hour of exposure to electromagnetic field at 900 MHz modulated by human voice could have an effect on the excitation-contraction coupling mechanism of mammalian fast- twitch skeletal muscles [13]. However, no study to date has investigated the effect of electromagnetic waves emitted by GSM relay antenna on muscle composition. Consequently, this study is designed to investigate the effect of 25V/m of electromagnetic waves emitted by GSM relay antenna on animal body weight, muscle mass, proteins and water content, total RNA expression, serum testosterone level and myosin heavy chain isoforms expression in the two types of skeletal muscle fibers, slow and fast- twitches.

This paper studies the effect of GSM waves on skeletal muscles. A background of the study is given in Section I. The materials and methods used in the study are mentioned in Section II. The results are presented in Section III, and discussed in Section IV.

II. MATERIALS AND METHODS

A. Experimental Design

All procedures in this study were performed in accordance with the stipulations of the Helsinki Declarations, and with the current Lebanese laws for animal experimentation. Twenty adult Sprague-Dawley male rats with an average weight of 190 ± 5 g were divided equally into 2 groups. One group was subjected for 6 weeks to whole continuous (24 hours/day) body exposure to EMW (900 MHz, E_{eff}= 25V/m). The other group was considered as control and maintained in the same environmental conditions under the turned off antenna. Both exposed and control animals were housed in a temperature-controlled room (22ºC) on a 12:12-h light-dark cycle. They were daily supplied with the same kind of food and water.

B. Dissection

After the exposure period, the rats were gently sacrificed and trunk blood was collected. Soleus and *edl* muscles were rapidly excised from the hind limbs of each rat. The muscles are weighted and preserved at - 80ºC for later analysis.

C. Total RNA extraction

Total RNA was extracted from muscle samples using **RiboZol™ RNA Extraction Reagent** from AMRESCO, according to the vender's instructions (American Research Products, 30175 Solon Industrial Parkway, Solon, OH 44139-9827 USA).

D. Serum testosterone level determination

Collected blood was centrifuged at 3500 rpm for 5 minutes. Serum of each rat was preserved at -20°C. Serum Testosterone levels in control and exposed groups were measured by Enzyme-Linked ImmunoSorbent Assay (ELISA) technique based on the principle of competitive binding, according to instructions supplied by the vender.

E. Proteins dosage

Protein dosage was performed according to Bradford Technique [14]. Pieces of frozen muscles were mechanically disrupted and spliced in 5 volumes of washing buffer containing 20 mM NaCl, 1 mM EGTA (pH 6.4), and 5 mM PO4. After 5 minutes of centrifugation at a high speed (12000 rpm), the supernatant is collected and the quantity of the protein is determined with the Bradford method (Bio-Rad, Hercules, CA), where the results were expressed as a ratio of milligrams of proteins to 100 milligrams of muscles. The pellet was then washed with 3 volumes of extraction buffer containing 5 mM EGTA, 1mM dithiothreitol (pH 8.5), and 100 mM sodium pyrophosphate, and incubated in cold overnight. The next day, the mixture was centrifuged at 12000 rpm for 10 minutes and the supernatant − which contained the protein myosin − was collected and the amount of myofibrillar proteins was determined. Small volumes (50μL) of the supernatant were diluted twice with glycerol and stored at -20°C for electrophoresis.

F. SDS-PAGE electrophoretic separation of Myosin Heavy Chain isoforms

To analyze the content of MHC I, MHC IIa, IIb, IId/x isoforms in the extracts, we used simple vertical migration of SDS-PAGE electrophoretic separation. The separating gel was prepared from 99.5% glycerol, 30% acrylamide, 0.6% bis acrylamide, 1.5 M Tris (pH 8.8), 1 M glycine, 10% SDS, 10% ammonium persulfate, and TEMED. The staking gel was prepared from 99.5% glycerol, 30% acrylamide, 0.6% bis acrylamide, 0.5 M Tris (pH 6.8), 10% SDS, 0.1 M EDTA (pH 7), 10% ammonium persulfate, and TEMED. For best quantification, 2-3 μg of myosin were loaded in each well. Electrophoresis was performed using a Cleavage, Scientific ltd, system. Gels were run at constant voltage (70V) for 24 h and then stained with silver reagent that allowed the detection of the MHC bands corresponding to I, IIa, IIb, and IId/x isoforms. The stained gels were scanned using a Canon digital imaging system and the density of bands was estimated using the UN-Scan-IT software [15].

G. Statistical analysis

All values are expressed as means $\pm$ SE for n observations. Data were analyzed by One-Way ANOVA (StatView; Alsyd, Meylan, France) statistical test. A level of $p< 0.05$ indicated statistical significance.

III. RESULTS

A. Effect of GSM waves exposure on Body mass

As shown in Fig. 1, all animals steadily gained weight and there was no difference observed between the control and exposed animals after 6 weeks of GSM waves exposure (Control: 283 ± 8 g; Exposed: 295 ± 7 g, n=10)
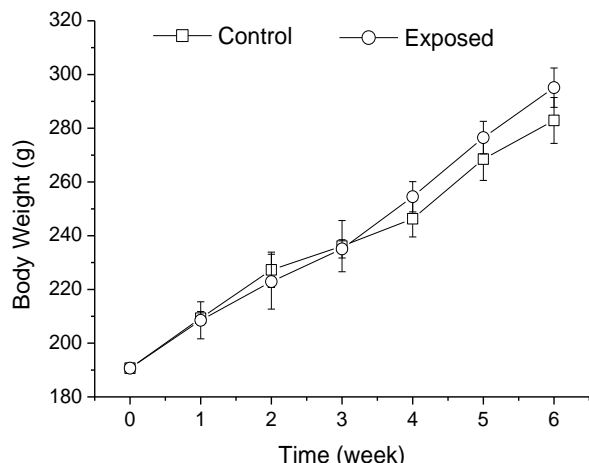

Fig. 1. Effect of GSM electromagnetic waves exposition on Body mass. Each value displays mean ±SE.

B. Effect of GSM waves exposure on muscles mass

Although body weight was not affected by the exposure, six weeks of exposure resulted in a significant decrease in *edl* mass by 16% (Control; 133.56 ± 3.69 mg; Exposed: 112.19 ± 2.57 mg, n=20, p<0.05). However, no significant effect was observed in soleus muscle mass (Control; 120.06 ± 2.89 mg; Exposed: 117.49 ± 3.11 mg, n=20) (Fig. 2).

Such a decrease in muscle mass observed in *edl* muscle could be related to modification in water content and/or in the proteins content. Consequently the water content and the soluble and myofibrillar proteins content were estimated.

C. Effect of GSM waves exposure on muscles water content

In control group, water content expressed as percentage is estimated to $37.5 \pm 0.7\%$ in soleus muscles and $26.9 \pm 0.6\%$ in *edl* muscles. After 6 weeks of continuous electromagnetic waves exposure, and although no significant effect was observed in soleus muscle mass, an increase by 17% in percentage of water content was observed ($43.9 \pm 1.2\%$, n=12, p<0.05). However, no significant effect was observed in *edl* muscles ($28.1 \pm 0.6\%$, n=12) (Fig. 3)

D. Effect of GSM waves exposure on proteins content

In soleus control muscles, soluble and myofibrillar proteins content were 2.71 ± 0.13 and 3.42 ± 0.26 mg/g of muscle, respectively. The six weeks of continuous electromagnetic waves exposure induced an increase by 23% of soluble proteins (3.34 ± 0.16 mg/g, n=24, p<0.05);

however, a decrease by 32% of myofibrillar proteins was observed (2.33 ± 0.29 mg/g, n=24, p<0.05) (Fig. 4).

In *edl* control muscles, soluble and myofibrillar proteins content were 3.56 ± 0.18 and 3.83 ± 0.11 mg/g of muscle, respectively. Six weeks of continuous GSM waves exposure induced a decrease by 28% and 24% of soluble and myofibrillar proteins, respectively (Soluble proteins content: 2.78 ± 0.19 mg/g; Myofibrillar proteins content: 2.91 ± 0.22 mg/g of muscle, n=24, p<0.05) (see Fig. 4).

These modifications in proteins content in both soleus and *edl* muscles should be correlated to total RNA level expression.
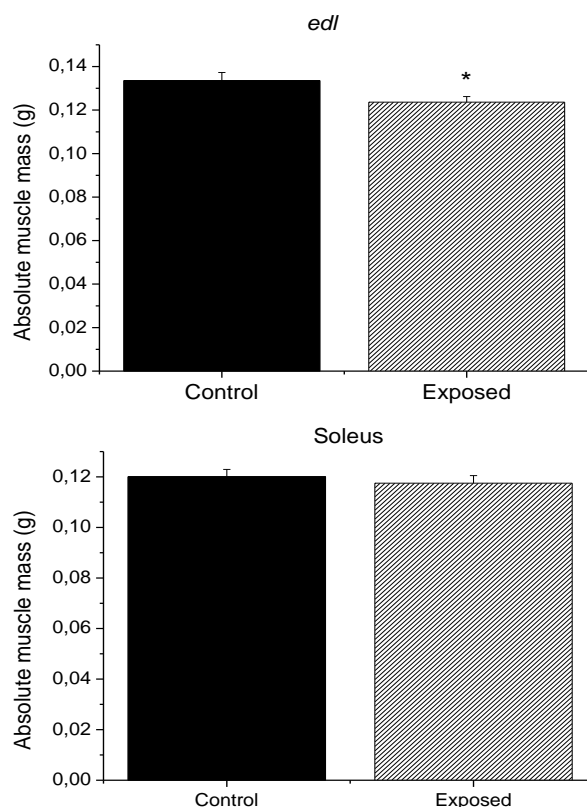

Fig. 2. Effect of GSM waves exposure on muscles mass of the *edl* and soleus muscles. Each histogram displays mean ±SE. * p < 0.05

E. Effect of GSM waves exposure on total RNA

In control condition, the total RNA values were 755.21 ± 16.72 μg/μl and 548.32 ± 14.98μg/μl in *edl* and soleus muscles, respectively. After 6 weeks of GSM exposure, a decrease by 29% and 25% were shown in both *edl* and soleus muscles, respectively (n=10; p<0.05).

This decrease in the amount of total RNA expression could be related to the modification in the serum testosterone level.

F. Effect of GSM waves exposure on serum testosterone level

In control condition, the Enzyme-Linked ImmunoSorbent Assay showed that serum testosterone level was 82.12 ± 4.39 ng/ml. Six weeks of GSM waves exposure induced a decrease by 50% in serum testosterone level (40.91 ± 5.71 ng/ml, n=10, p<0.05).

G. Effect of GSM waves exposure on Myosin Heavy Chain Isoforms expression

Separation and analysis of MHC isoforms by SDS-PAGE allowed the estimation of the density of the bands corresponding to each of the MHC isoforms (MHC I, II_a, II_b, and II_x) using the UN-Scan-IT software. These isoforms are differentially expressed in the different muscle fiber types. In control conditions, the *edl* muscle expresses 34.6 ± 0.2 % of MHC IIx and 66.4±2.8 % of MHC IIb, while the soleus muscle expresses 5.1 ± 1.7% of MHC IIa and 94.6 ± 1.5% of MHC I.

The 6 weeks of GSM waves exposure induced, in *edl* muscle, a significant increase by 63% in the expression of MHC IIx isoforms (56.3±4.2%) and a significant decrease by 33% in MHC IIb isoforms expression (44.9±3.4%, n=24, p<0.05).

Moreover, in soleus muscle, the exposure induced a significant increase in the expression of MHC IIa isoforms (16.1 ± 1.7%) with a significant decrease in the expression of MHC I isoforms (84.3±1.5%, n=24, p<0.05). (Fig. 5)
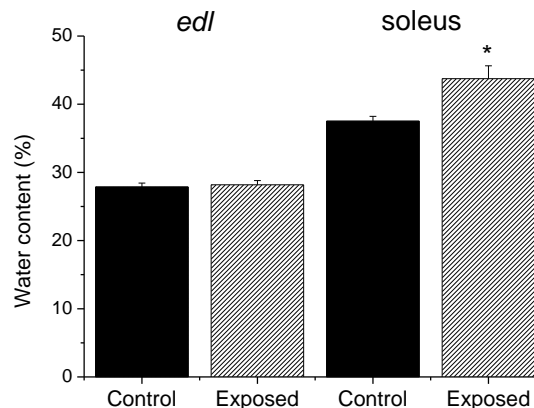

Fig. 3. Effect of GSM electromagnetic waves exposition on muscles water content of the *edl* and soleus muscles. Each histogram displays mean ±SE. * p < 0.05
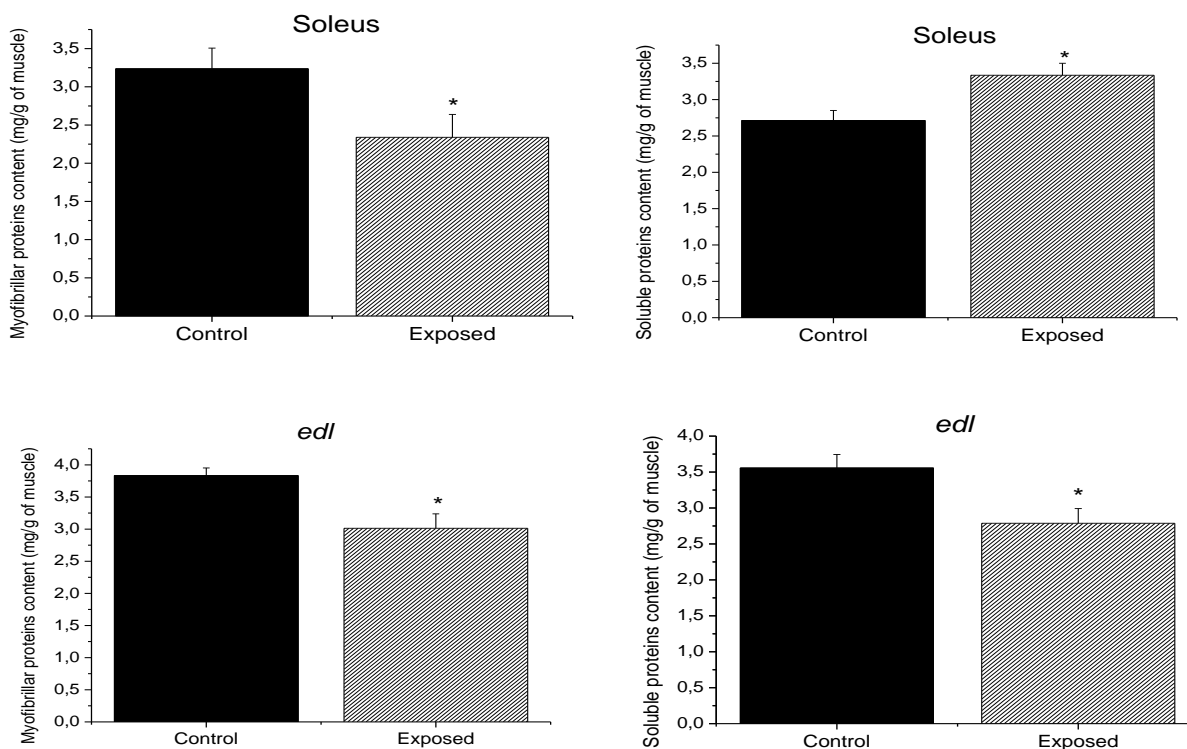

Fig. 4. Effect of GSM waves exposure on Myofibillar proteins content and soluble proteins content on both soleus and *edl* muscles. Each histogram displays mean ±SE. * p < 0.05
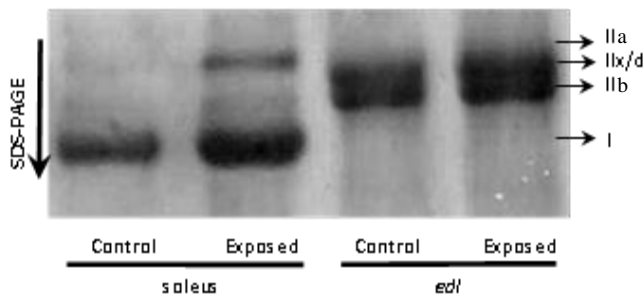
Fig. 5. Separation and analysis of MHC isoforms by SDS-PAGE in soleus and edl muscles in control rats and in rats exposed to 6 weeks of GSM waves. This figure show the bands corresponding to each of the MHC isoforms (MHC I, IIa, IIb, and IIx/d)

IV. DISCUSSION

Skeletal muscle is the most abundant tissue in animals representing up to 50% of body mass in some athletic species such as dogs and horses. Muscle fibers are composed of myofibrils arranged in parallel which constitute the major compartment in muscle cells, comprising from 73.2% of muscle fiber volume in horses to 83.3% of muscle fiber volume in goats. Also, total myofibrillar volume is directly proportional to muscle mass with a scaling factor of 0.98 [16].

This study aims to examine the effect of electromagnetic waves emitted from GSM antenna relay, at 900 MHz frequency, on body weight, muscle mass, protein content and the expression of the isoforms of the myosin heavy chain (MHC) in 2 types of muscle fiber types. One is slow oxidative fiber and the other is fast glycolytic fiber.

Many questions were raised about the possibility that exposure to electromagnetic fields emitted by mobile phones or their base stations could affect the health of users. If there is a health impact, there will be a global impact because the number of active cell phones is estimated to reach 7.3 billion by 2014. For this, the World Health Organization (WHO) established the International EMF Project in 1996 to assess the science, and recommended research to fill gaps in the knowledge of risks arising from exposure to electromagnetic fields on health [7].

Human skeletal muscle is a highly heterogeneous tissue, able to adapt to environmental challenges to which it is subjected. This process is governed by a set of mechanical, hormonal and nutritional signals [17-19]. Phenotypic plasticity of muscle tissue allows it to be modified in order to meet the specific demands faced by an animal during its life [13]. This critical property leads to a conversion of muscle fibers from slow to fast or vice versa [2, 20]. A wide range of contractile properties are mainly attributed to the diversity of the isoforms of MHC, which can exist in different muscle fibers. Four MHC isoforms (I, IIa, IIx and IIb), each encoded by a separate gene can be expressed in adult skeletal muscle. The intrinsic differences in the properties of the ATPase of MJHC isoforms led to the classification of fiber muscle as slow or fast fibers [18].

Generally, the fast-type genes appear to be expressed at birth, while the slow-type genes are expressed in response to changes in activity during development [17].

Actually, only two studies have examined the effect of electromagnetic waves on the skeletal muscle. The first study was conducted in vivo and showed that the field of microwave of 2.45 GHz has a stimulating effect on the activity of the muscle fibers, which is in part due to its non-thermal specific properties [12]. The second study was conducted in vitro, and showed that one hour of exposure to 900 MHz of electromagnetic field modulated by the human voice could have an effect on the mechanism of excitation-contraction coupling of skeletal muscle fast-twitch [13].

The results of our present work show that electromagnetic waves do not affect the body weight of rat males. In addition, the exposure period results in a decrease in absolute edl muscle mass, while that of soleus is kept unchanged. The myofibrillar protein content is directly proportional to muscle mass. A decrease in the mass of the edl was translated by decrease of both myofibrillar protein content and soluble protein. The increase in soluble protein content in soleus muscle was compensated by the decrease of myofibrillar proteins content resulting in the maintenance of muscle mass of soleus. This can be explained by the compensatory mechanisms at the translational and post-translational levels as suggested by Nikolova et al. [22]. In addition, synthetic modification in myofibrillar and soluble proteins in edl and soleus may be the consequence of the changes of level of transcription of genes encoding these proteins or due to perturbation in the stability of their corresponding mRNAs [20]. Therefore, the quantification of the mRNA encoding the soluble and myofibrillar and measurement of protein half-life is necessary to detect the level at which the change has led to modify the level of myofibrillar proteins and other proteins expressed in these two types of skeletal muscles. Our results provide new information by showing a decrease in the total RNA values in both edl and soleus muscles after 6 weeks of exposure to GSM.

On the other hand, the effect of electromagnetic waves is specific and can be attributed to a modification in the activity of different hormones. In 2010, Meo et al. [23] showed that exposure to radiation emitted by mobile phone for 60 minutes / day for a period of 3 months significantly decreased the level of serum testosterone in albino rats Wistar. In 2008, Al-Akhras showed that exposure for 6 weeks in a sinusoidal electromagnetic field of 50 Hz resulted in a significant reduction in levels of gonadotropins (FSH and LH) in female rats [24]. These results are similar to our results, where we showed a decrease in the level of testosterone after 6 weeks of exposure to GSM waves. This decrease can explain the decrease in total RNA values in both muscles since it is known that testosterone binds with androgen receptors inside the nucleus of different target cells and turn on the synthesis of mRNA which are then translated into specified proteins. Thus, the decrease of the

level of testosterone may explain the decrease of the RNA levels.

The change in the percentage of MHC isoforms was also detected. The results show an increase of the MHC IIa isoform, but a decrease in the MCH I isoform in the soleus muscle. In the edl muscle, a significant increase in MHC IIx and a significant decrease of MHC IIb isoforms were observed. These results suggest that the GSM antenna relay affects the plasticity of skeletal muscle fiber by transforming slow type to faster one.

Acknowledgments

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Stereo 3D Displays and Telemedicine

How to Select Stereo 3D Technology for Telemedical Applications

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Abstract — **The aim of this paper is to present some ideas and results of a current research related to using stereoscopic equipment meeting the requirements of telemedical applications. The target of the presented preliminary tests and investigations are 3D teleconference and telepresence. This investigation is the result of joint work with physicians from the Medical University Sofia.**

Keywords-stereo 3D display; telemedicine; active glasses; passive glasses; autostereoscopy

I.   INTRODUCTION

Telemedical applications have the potential to reduce differences in the people's quality of life because they allow the treatment of patients over long distances. This is the main goal of Telemedicine - to provide permanent and rapid access to physicians at distance using telecommunications, computer and information technologies, regardless of the patient's and the physician's locations:

- E-Doctors at telemedical centres (via telemedical equipment) offer easy and almost immediate or at least very simple access.
- It is quite common for serious medical conditions to be diagnosed at a later stage because it is often difficult for patients in rural areas to travel to large cities to get medical consultations in a tertiary hospital. Telemedicine enables and/or increases the access to an expert physician.
- Patients may require further monitoring and consulting after the treatment they have received in hospital at their first visit. Telemedicine is becoming a reasonable alternative to hospital physician visits and helps monitor chronic conditions. This increases patient's mobility and quality of life in post-hospital stages of the treatment.

Using up-to-date technologies is of crucial importance for telemedicine. The video, as a kind of data and information exchange and/or communication, has an important role in videoconference and telepresence [1].

Three-dimensional (3D) graphics has created new possibilities to present visual data and information. These opportunities add many new ideas in the field of Telemedicine: the 3D visualization of human internal organs of the human in their actual size and shape, and the analysis and manipulation of 3D structures from the captured 3D image(s). This is significant for a number of diagnostic and therapeutic applications, but this is an off-line activity. Surgical telemonitoring, emergency telemedicine and telepsychiatry are examples of the medical activities that require real-time action. The real-time 3D vision is one of solutions to increase the quality of these medical activities.

Though the term "3D" is ubiquitously used today, one can find two types of displays/monitors on the market: stereoscopic and holographic.

- Stereoscopic (binocular) vision is the result of the fusion of the two images (an image per eye) in the brain: although two eyes look in the same direction, they deliver two slightly different perspectives of the scene. Convergence, focus and physiological diplopia are the three components of stereoscopic vision.
- Holographic displays have the ability to provide all four eye mechanisms [6]: binocular disparity, motion parallax, accommodation and convergence. For marketing purposes or other reasons, the term 'holographic display' is often misused and applied in some cases to name systems, which are not truly holographic in the sense of video-holography. Even volumetric displays that create light spots somewhere within their volume are called in many cases 'holographic' [5].

The most notable difference between these two types of stereo 3D displays is that the observer lacks any freedom of head movement and the freedom to increase the amount of information about the 3D objects in the scene: holographic displays do not have this limitation but on the market the term "3D" is used to refer to stereoscopic 3D (dual 2D images as being "3D").

The ideas and results presented in this paper concerning the characteristics of current stereoscopic 3D displays are part of our joint projects and collaboration with physicians from the Medical University Sofia. We are investigating and testing some of the available systems and displays, and analyzing their characteristics and abilities for telemedical purposes. These activities are based on the aims and

objectives corresponding to the government strategy "2020" concerning Telemedicine.

This present paper is structured as follows. Section II looks into the pros and cons of current stereoscopic display technologies. Section III analyses the opportunities for a new type of imaging provided by 3D stereo technologies in telemedical applications. Section IV presents the conclusion.

II. PROS AND CONS OF CURRENT STEREOSCOPIC DISPLAY TECHNOLOGIES

3D photography gives an impression of depth, which is less convincing than real life. People looking at a stereoscopic picture may find that the third dimension only develops slowly. The longer they look, the more computation the brain does and the 3D impression improves with time. Stereoscopic vision is partly a learned response [7]: those who have looked at many 3D pictures seem to handle the computations with increasing rapidity. In fact, all visual interpretation is learned in infancy, especially the binocular interpretation.

Having in the three basic components of stereoscopic vision (convergence, focus and physiological diplopia) the following problems can be considered:

- Proprioception: the eye muscles must give accurate information about which direction the eye is oriented to.
- The eyes alignment: when looking into the far distance the optical axes must be parallel if the eyes are aligned correctly.
- The movement parallax cannot be used to sort out areas when viewing photographic stereo pairs.
- The dominant eye vision: the brain must not suppress the image obtained from one of the eyes.
- The eyes "autofocus" and 3D information: focus does not give 3D information although the eyes automatically focus to prevent the world becoming a blur. This is the result of the difference between the convergence information about distance and the sharpness of the image (the eyes lenses change shape independently, until the blur is removed). Stereo pairs are always presented on a flat surface and so, focus information and binocular information are never in agreement, which is a defect of stereoscopic displays.
- The brain training: the 3D impression from bumping into things and manipulating them can combine with binocular visual information.

Nowadays, three main versions of "3D" (stereoscopic) technology are of interest to the market:

- Active Stereo 3D: Shutter glasses are used to produce the 3D effect for the user and actively separate the images seen by the left and right eye.
- Passive Stereo 3D: There are two types of passive systems on the market.
  - Some passive displays are created using dual display technology: two displays present images with different polarization, and they are typically aligned with a half-mirror that permits the light from both displays to be presented together to the user's eyes. This approach allows stereo images to be presented to the user with full brightness and full resolution but it is too expensive.
  - The single display method is a more common method: special films are applied to the screen instead of producing 3D effect, and polarized glasses separate the images for the left and right eye.
- Autostereoscopic 3D: This means that no glasses are required.

For decades the Active Stereo 3D technology has been the standard solution for stereo 3D molecular visualization on the desktops and is still widely used. Many manufacturers use this technology. It is strongly promoted by NVIDIA with "3D vision technology" for desktop LCD displays [10]. Today for computer monitors AMD also offers a similar method, and for the LCD TV Samsung, Sony and Panasonic use this technology as a preferred method of delivering 3D to consumers.

There are several factors that should be taken into consideration when this technology is used. From computer engineering, point-of-view the pros and cons of the Active Stereo 3D technology are:

- Pros:
  - A 120 Hz input frequency: This helps to improve objects motion on LCD displays and to smooth high-speed motions (the perception of motion increases). It also helps users running competitive or high end computer graphics applications.
  - The full HD 3D: the full 1920 x 1080 resolution (of a 1080p image) is transmitted to each one of the eyes.
- Cons:
  - There is no defined industry standard at present, which means that maybe each pair of glasses (and vendors' methods) will only work with a small set of compatible devices, and not when paired with other vendors equipment.
  - Crosstalk: Overlapping of the left-side and the right-side images. As a result some times 3D images can look artificial.
  - Eye Fatigue: High input frequency flickers are part of this technology. Users don't see flickers, but the brain understands that flickers exist. This can lead to eye fatigue, dizziness and/or even headaches.
  - Image brightness: The brightness of the image is reduced when comparing 2D content with a 3D image (as a result, active glasses are already tinted).

The Passive Stereo 3D (the so-called polarized 3D) is oriented to glasses that aren't the active element in the creation of the 3D content on the display: glasses handle

polarization of the generated image to uncouple images for the left and for the right eye. This is based on the idea of the projection of two images (one for the left and one for the right eye) onto the screen and the use of polarization in a different direction for each image. The main manufacturer oriented towards this technology for the production of monitors/TV's is LG (Film-type Patterned Retarder (FPR) technology [8]).

From computer engineering point-of-view, the pros and cons of the Passive Stereo 3D technology are:

- Pros:
  - Glasses are very cheap: they do not need additional electronic and power supply.
  - This is a flicker-free technology: glasses don't receive 60 flashes per second. As a result, many users find these displays easier to look at for prolonged periods of time.
  - Image brightness: the brightness of the image is higher when compared to active stereo 3D.
  - Each of the eyes receives a non-breakable light stream.
  - No crosstalk: this technology separates left and right images more purely.
- Cons:
  - Aliasing and resolution of image: each eye is exposed to every second line of resolution (half of the frame) by this technology. It is a significant detractor from image quality (small objects and fine details are strongly affected by this) [9]. The closer you get to the screen, the more obvious this effect becomes. The loss of resolution is more pronounced for computer displays than it is for 3D TVs.
  - Motion blur: 60 Hz is the standard input for this technology and sometimes this produces perceived motion blur. Recently, to reduce this, manufacturers have started to announce 3D TVs with 240 Hz input.
  - View angle: the polarized filter is the active element for this technology and it is placed on the screen. This means the device has an optimal viewing angle (severe anomalies like ghosting start cropping up, making the output intolerable).

Autostereoscopic 3D displays are special displays which allow many different types of 3D content (objects, pictures, videos, animations) to be seen spatially in 3D: glasses free 3D visual technology. This is achieved by the so called parallax barrier technology and elements that make sure that each eye of the viewer sees a slightly different perspective. Nowadays, there are two main types of devices on the market:

- Single Viewer: devices work with two perspectives built up approximately 70 cm in front of the display.
- Multi Viewers: a number of different perspectives are projected in front of the screen. Since these perspectives are horizontally spread, many users can see a 3D image irrespective of the position in front

of the screen while standing/sitting comfortably around the display.

From computer engineering point-of-view, the pros and cons of the Autostereoscopic 3D technology are:

- Pros:
  - Glasses free technology
  - Resolution per eye: compared to other 3D display technologies the 'Single viewer' autostereoscopy has a higher reachable resolution per eye and gives a better image separation of the different perspectives. For many applications where 3D precision is a key factor this feature is a major advantage: this provides the possibility to create content with a higher depth disparity and/or very low depth differences can also be visualized spatially.
  - It is really possible to walk around an object based on the 'Multi viewers' autostereoscopy.
- Cons:
  - They are prohibitively expensive at the moment.
  - No standard: manufacturers are oriented to a short list of video-card vendors.
  - The time for training users to view stereo 3D is longer compared to other technologies.

The comparisons and characteristics presented in this section are not aiming at an exhausting overview of the existing technologies, but they are provided to help non-technical people to receive in-depth information concerning 3D imaging devices.

III.   TELEMEDICINE AND 3D STEREO TECHNOLOGIES

For Telemedical purposes video is used as a kind of data and information exchange and has an important role for videoconferencing and telepresence [1]:

- The main goal of video-conference applications in Telemedicine is to provide real-time visual and audio patient assessment. This type of applications was developed to connect physicians with patients located in isolated areas where climatic or geographical conditions render provider or patient transportation difficult and costly, resulting in inequalities in patient care. Teleconsultation, telepsychiatry and tele-education are well-known examples.
- In general, Telepresence means projecting virtual images of the operative field to remote sites. Surgical telementoring, teledermatology, teleophtalmology, teletrauma, and emergency telemedicine are some of the examples of telepresence practice in telemedicine.

Unfortunately, we were not able to find any overview of 3D imaging subjective perception and comparison of available 3D imaging technologies related to this case.

Two elements of the current video communication technology have critical importance for Telemedicine: peripherals (sensors, devices) and the video-audio-data transfer.

Our tests and analyses show that video-audio transfer is not the major problem for using new 3D vision technologies in Telemedicine: today's technology allows transferring of high-quality video and audio data over extremely short delay times (latency).

The main problem is with the devices. We split our investigation into two separate directions: devices for capturing real 3D and devices for 3D visualization. During the tests we ascertained the fact that the input of the 3D visualization device is the dominant characteristic for the 3D vision system.

The first part of the tests was oriented to 3D capturing devices. We investigated 3 different technologies for capturing 3D content and its transfer to the output device (different 3D displays). The additional information for that can be found in [2].

The second part of tests was oriented to 3D displays. We investigated and analyzed the existing information about available computer displays from the described above three main groups: with active glasses, with passive glasses and glass-free displays. The evaluation procedure of the result was expert-based: we used physicians to evaluate the quality of the 3D display and the ability to use them for medical purposes.

The next element for testing was the perception evaluation of 3D images by users with different eye problems: our investigation was oriented to evaluate the influence of the ability to generate stereoscopic content on the display with classical eyeglasses. We started this group of tests because self-tests hinted that:

- The length of the time for training eyes to perceive a 3D content is different.
- There is a difference between understanding of the 'normal' perception of a 3D content when the convergence is changed from low to high, and when the parallax is changed from positive to negative.

We tested the following kind of users with eyeglasses: single lens (with low, middle and high diopters, with nearsightedness or farsightedness without or with astigmatism) or a progressive lens with middle value diopters.

The results from our two groups of tests can be summarized as follows:

- The glass-free technologies are the future of 3D displays for telemedical applications:
  - If we need a simulation of a 'tête-à-tête' visit, this technology will be the only solution.
  - If we need to simulate a walk around an object or a group of objects this technology will be the only solution.
  - The influence of eyeglasses manifests itself in the extension of training time to start a 'normal' perception of 3D content.
- If we want to use glasses-based 3D stereo displays the active glasses are more suitable for Telemedical application:
  - New technologies reduce flickers and crosstalk (example: the last generation of NVIDIA 3D Vision).

- The ability to show up small details and/or objects many times, determines the quality of diagnosis.
- The passive 3D stereo technology can be applied in education, teleconference, VR and other kinds of simultaneous activities: the architecture of this type of systems will be similar to that in [3][4].

IV. CONCLUSION

The movie "Star Wars" (1977) changed the understanding of computer graphics and animation. The industries that didvnot understand this lesson lost market positions dramatically.

The movie "Avatar" (2009) changed the understanding of 3D video and audio realism. Today, many industries change their 2D-based tools and applications to 3D- and 4D-based ones. This is the future and it is coming fast in our life. Telemedicine is part of this life and it is under pressure to shift its human interactions basis from 2D to 3D.

In this papers, we did not discuss one of the most important questions – how to educate people to understand 3D artificial images correctly. It is subject of other research work.

Our world is computer-based. We need to understand computer limitations and we need to understand the future of computer technologies. Doctors want to be only doctors (not technicians) but computer technologies can increase doctors' sensing. Researchers and industry need to create and implement new computer technologies for medical application that can increase the quality of the diagnoses and treatment. The presented here ideas, observations and results are part of this scientific and technological support.

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An Integrated, Web-Based, and Automated
Healthcare Institution Quality Management (HIQMA) System

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Abstract—**This paper describes HIQMA, an integrated, web-based, and fully automated healthcare institution quality management system. HIQMA includes many applications, starting with a quality handbook for the individual beneficiary organizations and not ending by the development of service guidelines. It is based on a result-proven design approach that will enhance medical and healthcare services. The different stakeholders are provided with a common framework for designing, implementing, evaluating and improving these services. The system is scalable in the sense that additional professional development tools based on the worked service guidelines can be implemented.**

Keywords—healthcare; quality management system (QMS).

I. INTRODUCTION

Constant upgrading of the quality of healthcare centers is a key priority at institutional, national, regional, and international levels. Recent charted European agreements placed the objective of increasing the attractiveness of healthcare institutions and promoting medical tourism [3] as a key objective along with quality improvement requirements (e.g., the EU-OECD agreement on healthcare indicators [1], EUPHORIC Project [2], etc.).

To achieve such key objectives, most of the current systems follow the classical methodology of cyclic planning, implementation, assessment and review, and examine the process as a relative and contextual concept. That process is depicted in Figure 1 [4]. The above approach is usually taken to avoid the creation of a pervasive and unequivocal definition of healthcare quality. An effectual Quality Management System (QMS) targets the systemic development and communication of a customer-focused mission, strategies, and action plans. Thereby, listening and responding to customers' needs and expectations, empowering employees to keep improving and increasing their satisfaction with their work processes and environment, and gathering and analyzing Key Performance Indicators (KPIs) to enhance organizational and process results are of

immense importance for the good governance of an institution [5].

Consequently, an integrated web-based Healthcare Institution Quality Management (HIQMA) system is required to improve the medical and healthcare services. The system attributes include many applications, starting with a quality handbook for the individual beneficiary organizations, continuing with the reformed professional training and advisory service concepts, and ending with the developed service guidelines. In addition, scalability and customizability are intrinsic requirements of the system. These attributes ensure that different stakeholders are provided with a common framework for designing, implementing, evaluating and improving these services.

This paper describes the functionality of HIQMA system as well as some of its attributes and services. Section II describes the system in details. Section III outlines the governance and standard compliance dimensions. Section IV presents some results and impact assessments. Further enhancements are described in Section V.

Figure 1. Classical methodology of cyclic planning.

II. TOOL DESCRIPTION

Managing quality performance requires a comprehensive approach that has a dynamic nature in terms of agility and customization. This becomes highly important when dealing with healthcare institutions as they must carefully consider and control their activities to ensure all quality requirements are met. The integrated web-based automated HIQMA system that we built has been designed to assist such organizations in implementing and maintaining this comprehensive approach by delivering tools structured around the ISO 9000 family of international standards for quality management taking into consideration the special needs and features for healthcare services [6].

HIQMA is a centralized management system that provides a portal to critical quality information and facilitates quality performance improvement through requirement tracking, notifications and real-time management reporting. It has been designed to streamline and automate quality management processes of any medical organization and assist in the effective implementation of wide quality initiatives on a "use per need basis". The software system is 100% web-based, highly configurable QMS that helps organizations track, analyze, and report on quality management in addition to streamlining existing processes and enforcing their application.

The system was deployed for the first time in Lebanon in early 2011. Since then, the system has been deployed in 7 medical institutions covering 3 private hospitals with 100+ bed capacity, 2 polyclinics and 2 medical labs. As a part of the system's development and evolution plan, a new version of the software is installed every 6 months in all locations. Typically, the new software releases include bug fixes, further enhancements and new features. In an attempt to ensure customer satisfaction and continuous quality improvement, an annual on-line customer survey is conducted. The survey is comprised of 20 questions covering 4 distinctive areas: functionality, compliance, efficiency and quality control. A quantitative scale of 1-5 is used with 1 being poor and 5 being excellent. In the first survey conducted in early 2012, a total of 5 institutions responded to the survey and an average score of 3.90 was recorded. In the second survey conducted in early 2013, a total of 7 institutions responded to the survey giving the system an average score of 4.36. This suggests that the system has evolved nicely and is a viable candidate for wider deployment and adoption by other medical institutes. In the next sections, the main features of the system will be described in further details.

A. Web-Based Application

From a technical perspective, the system is web-based, with all of its features and their respective functionality accessible through any web browser. It can be hosted inside the healthcare institute's Local Area Network (LAN) with open or closed access from outside the institute's premises. The system can also be hosted online using any preferred hosting service provider. In addition, it offers a deployment model for organizations preferring to outsource hardware and software maintenance. Worldwide roll-out of the system can be completed in less than 6 hours enabling users with a URL, username and password to access the system from – virtually – any Internet access point. According to recent findings, web-based interfaces reduce the learning curve of medical or administrative staff who can begin to work with the system shortly after installation and incorporate it in their daily tasks and activities [7].

B. Centralized Activities Management and Customization

Through a friendly Graphical User Interface (GUI), the system provides the user with a workplace that is easy to work with through a variety of summary screens, task menus and drop-down lists. These features are accessed by a regular user according to his/her assigned privileges and/or role(s).

A regular user may access a user specific task summary screen that summarizes the responsibilities in sequential order. Users can be presented with this screen upon login, ensuring single click access to their most critical information. Management personnel have access to a personalized menu that provides visibility over current activities and pending assignments of the medical staff tasks. Management system coordinators and senior personnel have access to a complete listing of tasks by location, department, region or corporation as a whole.

The system tracks "who" is doing "what", "when", "where" and "how". It doesn't just store this information; rather, it automates such information through notifications and tracking mechanisms. All tasks, forms and assignments can trigger an email notification to the appropriate responsible person. Every email notification includes a hyperlink that sends the user directly to the task detail screen within the system. This screen provides further instructions, downloads, as well as fields, to record activity completion and uploads related documentation. The system ensures nothing falls through the cracks with an escalating email notification feature. The system can be configured to escalate the email notification of tasks pending completion. This feature is extremely flexible and can be configured to send any number of emails to any number of people to ensure tasks are completed on time.

C. Embedded Forms and Processes

The application is pre-loaded with numerous forms, checklists and common processes for all the necessary activities that are common in almost all healthcare institutions. The availability of such material will help the user complete needed tasks and activities in a controlled manner where human mistakes are minimized. Detailed process description is always displayed whenever the user invokes or triggers any activity which involves that respective process. If multiple processes are involved within a specific operation, then all of them will be made available to the user for consultation and cross-checking. This makes the application a fail-proof approach, ensuring all quality compliance requirements are met.

D. Flexible Reporting

The HIQMA system is designed to streamline the flow of information throughout the healthcare institution. Institutions can mirror their hierarchical structure within the database, and this enables data to flow from a site, to a department, to a unit, to institute-wide, to regional or other locations in the case of multi-center organizations. Each location, division, department or other type of unit can manage its structures independently, and can have varying levels of hierarchy.

Data within the system will roll-up to appropriate management levels instantly in real-time without the need for lengthy manual traditional processes and procedures. The system has a centralized reporting tool that makes sharing information easy. Users at all levels of the organization can generate reports that summarize performance status and requirements. All reports can be generated in the most popular formats (HTML, PDF, .DOC or .XLS). Reports can be configured online through the web-based interface. A screen-shot capturing the reporting panel is shown in Figure 2.

E. Mobility

The user is provided with great mobility and agility where the system may be accessed from any computer or mobile device from anywhere as long as there is a connection to the hosting server (LAN, WLAN, or Internet). This provides the users with instant access to data at all times. Mobility certainly improves business performance, increases organizational efficiency and decreases response time.

F. Security

The system has a robust security management console that enables access to the modules, locations and functionality to be controlled for each user and user group. System administrators, who have access to the security module, can manage user access and the views available to user groups, as well as view the history of user visits. In addition, encryption of the user credentials and data is included upon login and throughout the authentication and authorization process.

The User/Permissions module of the system allows a top level administrator to assign permissions and roles for each user individually or as part of a security group. The functional permissions of each user are assigned based not only on the actions he/she is supposed to take, but also down to the data level he/she is required to manipulate. For example, two different users may have the same role and permissions but each can perform his/her permissions on a specified set or pool of data by department, patient, or others.

G. Multi-Lingual Suppport

The system has a dynamic user interface that is available in multiple languages. Newly translated interfaces are continually being added. The system currently supports English, French, Arabic and Farsi languages. The system
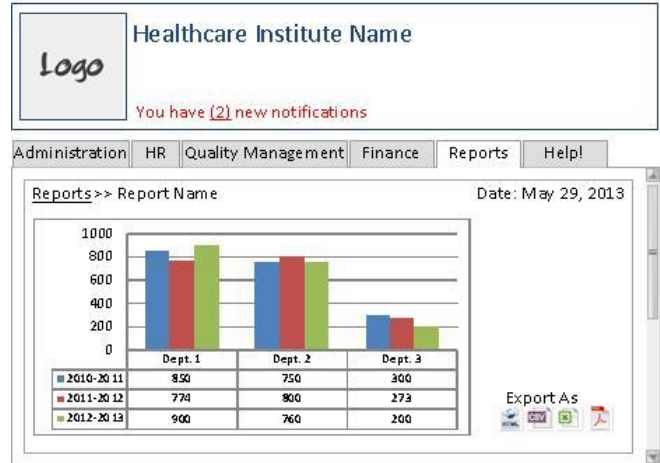

Figure 2.   Reporting panel screen-shot.

technology is developed in such a way that the interface's language can be changed by the user according to the languages requested by the medical organization. In addition, data entry in multiple languages is also currently supported. Although the system does not translate data, it does provide a centralized roll-up capability of data in multiple languages.

III.   GOVERNANCE AND COMPLIANCE

A. Governance

In any healthcare organization, small or large, adding, demoting, or changing forms and procedures is a procedure by itself. The users will require training on the new procedures and forms, and the printed documents require replacement to reflect new changes.

The system technical structure with respect to workplace, rules, forms, and menus takes into consideration future changes and enhancements of the business rules of the medical institution. Any updates to the forms or procedures are done directly on the system, and once committed, the institution ensures adherence to the new forms and rules instantaneously.

B. ISO Compliance

The software application is not only structured as per the ISO 9001 standards with all the modules that address each of its requirements, but also contains many unique features that facilitate on-going continuous improvements [8]. It is designed specifically for healthcare institutions implementing or maintaining a QMS based on ISO standards [9]. In addition, it drastically improves internal or third party audit results by adhering to the ISO modules summarized in Table 1 [10].

IV.   RESULTS AND IMPACTS

So far, the system has been recently deployed in a number of healthcare institutions in addition to a number of medical colleges and universities. Certainly, each sector has

TABLE I: A SUMMARY OF SUPPORTED ISO 9001 2008
REQUIREMENTS

ISO 9001 2008 Requirements	
Clause	Title
5.3	Quality Policy
5.4.1	Quality Objectives
5.4.2	Quality management system planning
5	Management responsibility
5.1	Management commitment
5.5.1	Responsibility and authority
5.5.2	Management representative
6.6.2	Competence, awareness and training
5.5.3	Internal communication
7.2.3	Customer communication
4.2	Documentation requirements
4.2.2	Quality manual
4.2.3	Control of documents
8.5.2	Corrective action
8.5.3	Preventive action
7.6	Control of monitoring and measurement devices
8	Measurement, analysis and improvement
8.2	Monitoring and Measurement
8.2.3	Monitoring and measurement of processes
8.2.4	Monitoring and measurement of product
8.3	Control of nonconforming product
8.4	Analysis of data
4.2.4	Control of records
8.2.2	Internal audit
5.6	Management review
5.6.2	Review input
5.6.3	Review output

its own flavor of the system but a number of common conclusions could be derived from their deployment and operations. Some highlights are:

- Seamlessly orientating the users to clearly understand and easily satisfy the quality needs.
- Continuing improvement in the institution by adopting quality as a philosophy. This is a crucial requirement for adopting a total quality management (TQM) approach which is essential for business sustainability.
- Presenting defined and consistent processes and guaranteeing their successful completion as long as processes are done in a timely manner according to the standards.
- Adhering to preventing instead of supervising, thus ensuring that the costs of preventive measures are

less than those of close supervision or micro-management. This is a proactive step rather than a reactive one.
- Utilizing a single, institution-wide system to manage all quality management information and initiatives. This becomes especially relevant in multi-location institutions.
- Automating the tracking, management, and notification of the QMS stakeholders.
- Providing web-based tracking forms, analysis tools, and roll-up reporting to facilitate continual improvement and measurement of key performance indicators.
- Centralizing the management of quality related activities and requirements and driving the medical institution performance.
- Experiencing robust document control and management for all quality related procedures and policies.

The outlined findings are based on preliminary on-line surveys that were done by the institutions where the system was deployed and on thorough discussions with the various stakeholders through the formal review and evaluation process. The following lessons learned were also noted:

- A common – and rather classical – issue is faced in most of the institutions, which is related to the resistance to change, especially in institutions where some staff personnel have a low adaptation capability to non-paper based systems.
- Changes and updates in automated quality management systems belong in general to the service/product provider which limits the capability and the capacity of the institution to abrupt changes in running processes which might be needed in some cases where non-ordinary circumstances are present (ex: change management in risky zones).
- For institutions with low number of patients and specialties, the cost of such a system will increase the overhead and somehow lower the quality/price ratio. Usually, such institutions are oriented towards systems with fewer modules, thus leading to a limited access to all the benefits of the system.
- Institutions with simple – or no – information technology (IT) departments will face the problem of hosting and managing the system servers. Such institutions are advised to go with the cloud hosting solution to minimize the overhead and transfer the risks to the hosting service provider.

Many institutions that deployed this system found the need to update some of their forms, rules, and procedures early in the definition phase. The structured and logical methodology the system uses can spot flaws in procedures and regulations. In addition, it allows the institution to do a major review on the consistency and integrity of its existing QM system.

V. FURTHER ENHANCEMENTS

The HIQMA system is open to a huge set of enhancements in the future. Currently, we have three main enhancement features and propositions being studied.

The first enhancement is to develop an add-on module to the system that is able to collect data from multiple institutions and organizations. This pool of data will result in a knowledge base that will allow the analysis of quality management practices on national or international levels. It will also give insights on how institutions interpret and understand quality, as well as propose best practices and procedures.

The other enhancement is to allow healthcare institutions with well-established IT departments the capability of creating and designing their own forms and workflow from a graphical interface without the need to write code.

A long-term proposition is to add a "Learn Mode" module powered with artificial intelligence code that reads and interprets the system's technical logs to automatically propose enhancements to procedures and policies. The "Learn Mode" can be set to individual parts of the system or to the whole set of enabled modules.

VI. CONCLUSION

The good healthcare service is not only a social responsibility, but also a good contributor to economic competitiveness and welfare in a global knowledge-based economy. Many challenges face medical services, including developing and upgrading the skills of the existing workforce, promoting labor mobility, diversifying customer base, and – most importantly – planning and implementation of education and training services. All of the above require that the management of such programs be handled with care and innovation, on the one hand to maintain a quality culture in the institution, and on the other, to keep up with a the competitive edge of the services rendered.

The integrated web-based HIQMA system can meet these challenges, and more. The system tackles the details of ISO standards and medical services peculiarities, and delivers a high quality, high performance package for use by the various institutes, irrespective of their specializations. Such an approach proved to be efficient, robust, and reliable in all the sites where it was installed and tested.

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A Model for Global Health Virtual Communities

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Abstract— **This paper presents a model for Health Virtual Communities deployed on a Global Health level. It starts with an initial model built previously, and provides a thorough analysis of the components needed on a Global Health level, in order to provide a successful Global Health Virtual Community. The model provides a list of characteristics that a Global Health VC design should have in order for it to provide a viable, value-added experience to the participants.**

Keywords-Community; Health; Global Health; Online Communities; Modeling

I. INTRODUCTION

In the beginning of the 1990's, people started to create online communities, also known as Virtual Communities (VCs). The phenomenon was due to the development of the World Wide Web. Researchers started to explore ways in which people use VCs. For instance, Kivimäki et al. [1] investigated interaction patterns and identity formation in a VCs including mechanisms that supported identity formation (awareness, voice, text, voice, authentication) [1, 2]. In later stages, the emergence of deviant behavior in VCs pushed the researchers to propose trust tools [3-5].The ways in which teams are formed inside a community were also analyzed and coordination [6] and awareness [7] emerged as determinant factors in team formation. Later on, both tacit and explicit knowledge in VCs [8] [9] were captured and used of in different domains [10]. Health related Virtual Communities did also emerge, with their own opportunities and challenges [11] [12].

However, very little has been the effort to address the issues related to Global Health Virtual Communities and Challenges. In this paper, we will overview these challenges and suggest a preliminary model for Global Health VCs.

In this paper, we will present a model for virtual communities in section II, and describe the types of global health virtual communities' challenges in section III. A global health virtual community model is described in section IV, and section V concludes the paper.

II. VIRTUAL COMMUNITY MODEL

We will take as a starting point a model for collaborative virtual communities that has been suggested by El Morr [11] [13]:

A. A Model for Collaborative VCs

Four dimensions characterize the model, shown in Figure 1: the degree of virtuality, the degree of mobility, the degree of cooperation and the degree of uniformity.

The degree of mobility specifies if the VC members is 'Still or 'mobile'

The degree of virtuality specifies if an encounter between members is 'physical' (members are physically in the same place) or 'virtual' (members meet online) .

The degree of cooperation specifies if the members' awareness of each other passes through a simple notification mechanism, or if the members 'collaborate' dynamically and actively on a common aim

The degree of uniformity specifies if the members are extremely 'homogeneous' (the VC is a community of practice); or 'heterogeneous' (having different occupations).
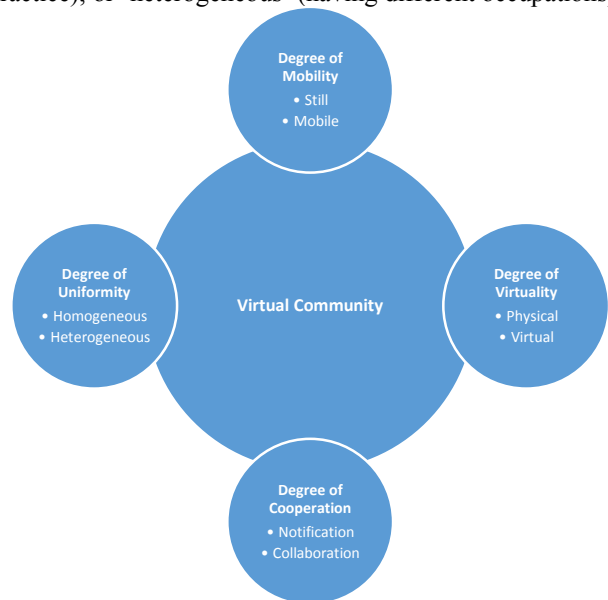

Figure 1. The four dimensions of a collaborative virtual community

This model is a generic one and we should update it to take into consideration the particularities of the health field and of the global dimension, inherent to a global health virtual community.

III. GLOBAL HEALTH VIRTUAL COMMUNITIES CHALLENGES

A global health virtual community presents particular challenges that should be dealt with in order for it to be successful. These challenges are related to the sensitivity of the health sector (e.g., confidentiality) and to the global reach of the community (e.g., cultures). In the next two paragraphs, we will analyze both of these types of challenges.

A. Health related challenges

A health VC could be patient centered, profession centered or dedicated for general public access.

Patient-centered VCs focus their activities on care delivery mechanisms to provide *support* for patients while they are away from the point of care. Patient support is important because social factors, such as isolation and lack of social relationships, have a tremendous impact on health. Research has shown that social factors have an effect on cold [14], coronary heart disease [15][16], cancer, hypertension, tuberculosis, cirrhosis of the liver, suicide, and death rate [17]. This explain the development of Health VCs that support patients with conditions such as HIV, Cancer [5, 18-26] and depression [27], and others that provide tele-monitoring capacity of patients at home [28][29].

On the other hand, VCs can be **Professional-Centered. Such VCs are dedicated** to *support professionals* in their activities around patients; they can provide knowledge sharing mechanisms [8, 30-33], enable knowledge creation and dissemination, or educate the public and non-governmental organizations [10].

Public-Centered VCs aim to educate the population (e.g., *self-management* of their disease), which empowers the public and affect positively their health [34-41] [42] [43]. In this context, mobile-based health care VCs is expected to play a key role in self-managed care [44].

B. Global Virtual Communities Challenges

A Global Health VC raises many challenges to the healthcare community. It shares some of these challenges with the local health virtual communities while it has specific ones tied to its global perspective.

1) Common challenges

Usability is still an issue in information systems development, and it is of paramount importance in healthcare. In Global Health VCs, it would be crucial to have a user interface built to enhance the user experience (e.g., patient, nurses, doctors, caregivers). The success of any global health VC is related to having a usable interface that enables users instead of disabling them. We shall call this an *inclusive design* in our model.

The other challenge is to build mechanisms to enable participation in the community; such mechanisms are essential to avoid lurking [45][46][47]. A *participatory approach* is then unavoidable.

Many failures in healthcare related information systems are related to the lack of members' support. A global health VC should be *Supportive*; such feature will boost adoption and minimize resistance to a disruptive technology.

The global health VC should also be able to integrate in the workflow in place. On a global level, the workflows of different participants may differ drastically, having to adapt to heterogeneous workflows is necessary for the global health VC to operate seamlessly in its environment. A *workflow adaptive* dimension in the global health VC is therefore important.

Security, trust, and privacy/confidentiality are important too; though, on a global level the question of data storage is sensitive. The geographical location where data is stored and the laws that would apply in case of a breach of confidentiality are global specific. However, this is a policy issue and not a mere technological challenge; policy mechanisms should be part of any global health VC model. Hence, the global health VC should be *policy sensitive*.

Finally, personalization of the information and the interface presented to the user are important so that s/he is not overwhelmed with information and irrelevant interface features. A *profile sensitive* VC would be necessary.

2) Global perspective challenges

Some of the global challenges in Global Health VCs are the cultural differences, the environmental features, the asymmetry in the infrastructure, and the perceived VC value.

A global health VC should adapt to many languages and possibly cultural differences. A successful global health VC should be *culturally adaptive*.
Users should acknowledge the differences in the local environments; for instance, a disease in one country may be irrelevant in another. The global health VC should be *environmentally adaptive*.

One of the challenges that may be faced is the asymmetry in infrastructural (e.g., a developed and a developing country may not have access to the same technologies). A global health VC should provide many channels for communication and cooperation, thus providing *technology adaptive* features.

All parties involved from different countries should be able to perceive value in the VC. The global health VC can achieve this aim by providing means to share resource between stakeholders. A fruitful global health VC should be able to be poised as a *value catalyst*.

IV. TOWARDS A GLOBAL HEALTH VIRTUAL COMMUNITIES MODEL

Based on the above analysis, we can adjust the preliminary model presented in figure 1 adding to it the features discussed above; the result is shown in figure 2.

Figure 2. A Global Health Virtual Community Model

A. A scenario

Consider an example of a global health virtual community project, involving a developed and a developing country, dedicated for chronic diseases self-management.

We will apply the above model to analyze the VC requirements and identify its high-level needs.

Degree of Mobility

Most of the parts of the system need not to be mobile. That includes a component of online education that can ne browsed on a PC/laptop/tablet. However, a mobile App should be provided for people having access to smart phones in both developing and developed countries. Besides, in the developing country, the e-education can take place using targeted SMS messages. For elderly, a DVD presenting the educational material would be most appropriate in developing countries. Thus, a hybrid approach would be chosen, to incorporate online, off-line, mobile and static access to the material.

Degree of Virtuality: The community would be virtual since members would not be connected to it virtually and they are not present in the same physical space.

Degree of Cooperation: Consumer members (i.e., patients) would need only loose cooperation. A forum would be enough if there were a need to connect patients together in order for them to exchange experiences. Administrators and researchers of the VC will require special tool to enable tight cooperation.

Degree of Uniformity: The community would be heterogeneous since it would involve patients, researchers, doctors, nurses, field workers, etc.

Design Inclusivity: The design would have to be inclusive since its inception. For instance, the patients can present different degrees of disability due to age and/or pathology.

Therefore, patients would be included in the design in early stages. Besides, there would be a need to decide on the languages used to present the educational material.

Participatory Approach: A participatory approach could be not needed since members would either seek participation for the sake of their own health (e.g., patients), or for the sake of providing healthcare advices and monitor the VC (e.g., researchers, doctors).

Supportiveness: A VC administrator could be needed to support the members using the system.

Workflow Adaptability: In this particular VC, the workflow is not an issue, since the VC is patient oriented and do not interfere with the day to day activities of the healthcare providers.

Policy Sensitivity: The privacy and confidentiality laws and regulations would be implemented based on the local laws and regulations of the host server (e.g. developed country). However, policies regarding data extraction and use should be set in place in order for all parties to be able to use data without confidentiality breaches.

Profile Sensitivity: The user interface should be adapted to the patient profiles. Age and pathology would be major factors in the adaptation process; for example, elderly would need a non-cluttered, simplified, user interface.

Cultural Adaptability: The researchers would have to use both languages in effect in both countries. Therefore, the educational material should be translated.

Environmental Adaptability: There was no environmental issue since the VC is educating patients having the same chronic diseases.

Infrastructure Adaptability: Researcher could decided on many delivery strategies for the educational modules. A basic cellular communication infrastructure in the developing country could dictate an SMS delivery method for mobile users of that country. While a 4G network in the developed country would lead to developing Apps for patients with smart phone devices. Many delivery channels would then be in place.

Value Catalyst: We could expect the VC to be perceived as adding value for patients in both developed and developing countries. Beside, healthcare and economic systems in both countries would benefit from the VC role in enhancing the patients quality of health.

B. Consequences

This scenario demonstrate how would the model be applied and how it would provide help in structuring the way we identify the high-level needs of a global health VC, leading us to ask the right questions and make the right analysis and design of the system.

V. CONCLUSION

This paper analyzed the virtual community features and the health field needs and challenges in a global perspective; it then proposes to enlarge a previous VC model to make it adaptive to a global health perspective. The model provides a list of characteristics a Global Health VC design should take into consideration to implementing a viable, successful, value-added experience to the participants in a global health virtual

community. We provided a scenario to demonstrate the ability of the model to guide developers through the analysis phase of a global health VC project, and to provide a streamlined way to identify a suitable course of actions.

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Nanostructured Porous Silicon Scaffolds for Biofuel Cells

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Abstract—**An Enzymatic biofuel cell is a specific type of fuel cell which uses enzymes as catalysts to oxidize its fuel. They pose as a great promise in terms of their relatively inexpensive components and fuels, as well as a potential power source for bionic implants. Here, we present the use of dry-etched nanotextured porous silicon scaffolds to increase the contact surface area of silicon with surrounding biofuel to enhance the process of harvesting of energy, and consequently, the efficiency of the cell.**

Keywords-nanotechnology; porous silicon; biofuel cell

I. INTRODUCTION

Recent advances in micro and nanotechnologies allow the development of implantable, portable, and miniature devices for a broad range of applications, including biomedical fields. Powering implantable medical devices necessitates the development of lightweight, non-toxic and stable sources of energy with long life spans. In fact, the number of battery charging cycles in micro-energy harvesting methods is a major source of limitation [1]. Several micro-energy harvesting sources have been already identified in previous research, namely, low and high frequency electromagnetic Radio Frequency (RF) signal harvesting, conversion of vibration into energy, thermal and pressure gradients energy harvesting in addition to the latest attempts towards organic energy generation directly within the human body using fuel cells [2, 3].

Harvesting energy using ambient vibration has been the focus of various projects [4-6]. Devices made for this purpose are mechanically modeled with a base excitation of an elastically mounted seismic mass moving past a coil. Optimal architecture for maximal power generation under different operating conditions has also been shown [7]. Various applications of this principle have manifested in systems integrated in footwear to harvest energy from walking [8], while in other designs piezoelectric and electromagnetic generators convert pressure variations into electricity [9]. The power generated using these methods ranges from tens to hundreds of milliwatts [3, 6, 7]. On the other hand, several studies have focused on energy harvesting from low frequency vibrations [6, 10]. This concept was made viable by creating a generator that converts low-frequency environmental vibrations to a higher frequency by employing the frequency up conversion technique [11, 12]. One major limitation of this technology is

encountered with patients that are not able to perform any physical activities in order to power the generator and, hence, produce the necessary charging current.

Energy harvesting using RF inductive coupling is a very promising technology, particularly in the presence of such a wide variety of RF signals in our everyday environment. Additionally, this technology can also be used to send data back to a base station, thus creating a two-way link. The system consists of a power generating circuit linked to a receiving antenna in order to capture the RF signal and convert it to a DC voltage [13]. The main challenge in this technology is in the receiver's capacity to read various frequencies, as well as the use of efficient power rectifiers. Several interesting studies have reported either the use of multiple energy harvesting antennas in one area [14], which has shown that an increase of 83% in area results in 300% increase in power, or the design of a high efficiency, ultra-low voltage active rectifiers [15].

This article covers the use of porous silicon scaffolds for biofuel cells. The next section presents and compares different types of biofuel cells. Section III introduces porous silicon technology. Section IV discusses existing porous silicon fabrication techniques. Section V details the fabrication process of the porous silicon scaffolds using XeF_2.

II. BIOFUEL CELLS

The first enzyme based glucose/O_2 fuel cell to generate electricity was introduced in 1964 by Yahiro et al., aiming at using this concept to power an artificial heart [16]. While the field of fuel cell research has flourished in various industrial and environmental arenas, biomedical applications started making use of the technology only after 2001, with recent successes in micro fuel cell technology [17-19]. The two most dominant classifications of fuel cells are enzymatic, illustrated in Fig. 1, and microbial, based on the catalyst used to oxidize or reduce the fuel used in the design [20]. While microbial catalysts offer more longevity to the fuel cell, microbial fuel cells require a barrier between the cathode and the anode and between the fuel cell and its surrounding environment [21]. Such a design increases its size and decreases the current density since the fuel cell lacks direct contact with the fuel. Most importantly, when it comes to the use of microbial fuel cell for implantable devices, long term infections, thrombosis and other types of complications raise serious concerns [22, 23]. Therefore, it is natural that the use

of microbial fuel cells was limited to few studies, one of them suggesting its use within the intestinal environment inside the transverse colon [24]. On the other hand, enzymatic fuel cells have lower stability and shorter lifespan because the longevity of enzymes is in the range of 10 days [25]. This has driven research in enzymatic fuel cells towards short term uses such as glucose sensors, post-op temperature measurement or as a power supply for pressure sensors indicating blockage of fluid flow in the nervous system [22]. However, since enzymes are selective in nature, the design of enzymatic fuel cells can be made into microscopic sizes without the need for a separating membrane to regulate the flow of the fluid and enzymes used in its design, thus achieving higher power densities due to the direct contact between the probes and the fuel [25]. Continuous attempts to increase the lifetime of the enzymes exist using immobilization techniques or using magnetic iron nanoparticles that shield the enzymes from getting oxidized or self-digested [26].
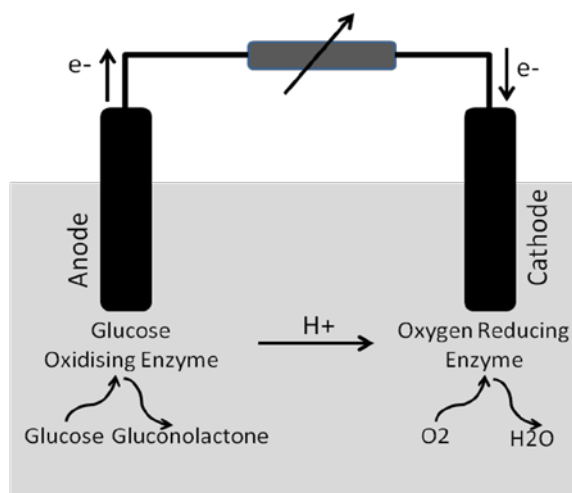
Figure 1: Illustration of an enzymatic biofuel cell using Glucose and Oxygen.

Another important factor in the design of the fuel cell is the target fuel. Although most implantable fuel cell studies have focused so far on the use of blood stream glucose, some studies have considered other alternatives such as the use of white blood cells based on their ability to generate electron current across their cellular membrane [27-29].

Most importantly, the complex environment inside the human body, such as the amount of glucose and oxygen available in addition to the neo-vascular build up that can hinder the exposure of the fuel cell to body fluids, represent important obstacles that any fuel cell design have to overcome in order for it to become a viable one [28]. Based on the first in-vivo study conducted by Cinquin et al., an enzymatic fuel cell was built by adjusting the types of enzymes used in order to account for the specific HP concentration and the effect of urea presence on the fuel cell [30]. This was implanted inside the peritoneal cavity of a rat, and has proven to provide a stable power of more than 7.52 μW/mL for a period of 3 months [30].

Here, we are interested in increasing the efficiency of energy harvesting in enzymatic fuel cells by increasing the contact surface area between the harvesting probes and the surrounding fuel. This can be achieved by using a porous interface which provides a large surface to volume ratio. Doped porous silicon represents a good candidate due to the fact that it combines both biocompatibility and electrical conductivity [31, 32].

III.   PorousSilcion Technology

Implantable biomedical devices built from bulk silicon have been available for biosensing and actuating applications for several years. However, this form of silicon is not biocompatible and so far this has prevented its use in vivo. Bulk silicon-based devices need coating or packaging in a biocompatible material, if they are to be used in and linked to living tissues [31, 32]. The majority of today's medical devices are coated with materials such as Polyvinylchloride (PVC), polypropylene, polycarbonate, fluorinated plastics and stainless steel. These materials are tolerated by the human body and are described as bioinert. An effective biomaterial, however, must bond to living tissue and is known as bioactive.

Nanostructured porous silicon (PS), whose particular texture can be described as a network of pores interconnected by solid nanocrystalline silicon, has properties that make it a very promising bioactive biomaterial [33, 34], in particular for devices that need to be linked to the biological system such as implantable devices [35]. Porous silicon material is useful and attractive for a wide variety of applications to develop biological sensors [35-37] and biomedical devices [38, 39]. This has significantly increased the interest in using porous silicon in biofuel cells.

An essential requirement for fabricating porous silicon in different applications is to have the ability to vary the size and configuration of the pores by choosing the appropriate fabrication parameters and conditions. For instance, for photonic bandgap filters, the pores are designed to the on the order of the wavelength of the light to retain and tune the optical reflectivity of the porous silicon [40, 41]. For biological sample filters, the pore size has to be large enough to allow the desired biomolecules to be filtered and cross through the pores freely [42].

IV.   Fabrication of Porous Silcon

Many previous reports have shown that porous silicon can be prepared through a galvanostatic, chemical, or photochemical etching procedures in the presence of hydrofluoric (HF) acid solutions or through stain etching [43-45]. Other methods such as pulsed anodic etching [46] and magnetic-field assisted anodization [47] were also employed for porous silicon preparation. In these techniques, the pore characteristics such as diameter, geometric shape and direction of the pores not only depend on the composition of the etching solution, but they also depend on temperature, current density, crystal orientation, dopant and doping density of the silicon substrate [43, 45, 48]. Moreover, porous silicon produced on large surface areas

along with high porosity and/or thickness leads to a systematic cracking of the layer during the evaporation of the etching solvent. The origin of the cracking is the large capillary stress associated with evaporation from the pores. During the evaporation process, a pressure drop occurs across the gas/liquid interface that forms inside the pores [49].

In this paper, we employ a novel and simple fabrication technique which employs Xenon Difluoride (XeF_2)-based dry isotropic etching to selectively form porous silicon in bulk single crystal silicon wafers [50]. XeF_2 is plasma-less etching technique and is based on the reaction of the fluorine ions, which represents the main etchant, with the solid silicon to produce – at room temperature – the volatile gas SiF_4. In a XeF_2-based etching process, a standard hard baked layer of photoresist can serve as a masking layer. In addition to its etching process simplicity, XeF_2 has a high etch selectivity to silicon. It reacts readily with silicon, but is relatively inert to photoresistance, silicon dioxide, silicon nitride and aluminum, which allows this technique to be used in the presence of CMOS integrated circuits as a post processing step. This is not the case when HF-based etching is used, as this latter will etch or damage the circuitry without a very hard mask followed by complex post-processing to remove the mask.

V. METHODS

We utilized XeF_2 dry etching to create porous silicon surfaces on single crystalline silicon wafers. We used 3 inch diameter, 381 ± 20 μm thick <100> boron-doped (5–10 ohm cm) silicon wafers. The wafer was cut into 1.3 X 1.3 cm^2 that were then loaded in the XeF_2 etching chamber. The XeF_2 etching process does not depend on the silicon crystal orientation or its dopant content.

The fabrication process is achieved in a sequence of steps. First, undissociated gaseous XeF_2 is adsorbed onto the exposed areas of bulk silicon. The adsorbed gas is then dissociated into xenon and fluorine, after which the fluorine ions react with silicon to produce SiF_4 gas. Dissociation of the gas phase at room temperature leaves behind a porous silicon surface. In this process, increasing the etching process time increases the overall size of the pores and the thickness of the porous silicon film. The chemical reaction for the etching of silicon by XeF_2 is: $Si + 2XeF_2 \rightarrow SiF_4 + 2Xe$. As a dry etching technique, there is no post-fabrication drying step required, thus reducing the risk of damage to the newly formed porous surface.

XeF_2 leaves behind porous silicon surfaces on top of the remaining bulk silicon with porous silicon layer thickness on the order of several hundreds of nanometers (600 to 700 nm). The obtained porosity depends on the etching time. Fig. 2 shows a representative Scanning Electron Microscope image of porous silicon sample prepared using XeF_2. "''

VI. CONCLUSION AND FUTURE WORK

Nanostructured doped porous silicon is a promising material for Biofuel cells. It offers several advantages including the use of silicon in microelectronics,
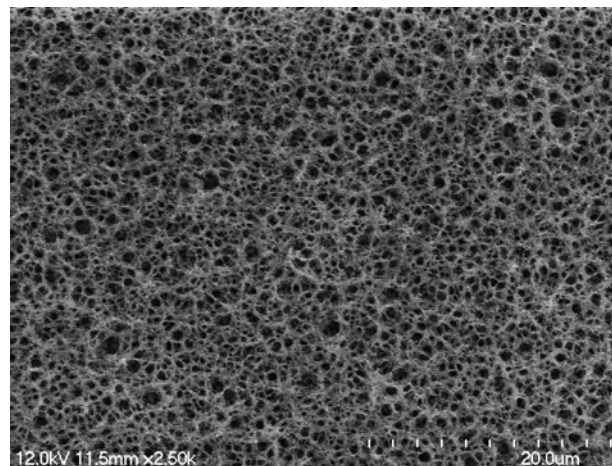

Figure 2: Scanning electron micrograph of a nanostructured porous silicon etched with XeF2.

biocompatibility, and simplicity in tailoring porosity and conductivity. Future work will focus on testing porous silicon samples in complete enzymatic fuel cell setup.

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Built-In Self-Testing Infrastructure and Methodology
for an EMG Signal Capture Module

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Abstract— **Wearable technologies introduce a refinement to personal monitoring by permitting a long-term on-person approach to physiological signals capture. Sensors, textile integration, electronics miniaturization and other technological developments are directly responsible for advancements in this domain; however, in spite of the present progress there are still a number of obstacles to overcome for truly achieving seamless wearable monitoring technology. That concerns, namely, the increase of system's reliability at the design stage, including the adoption of built-in self-test features able to detect functional failures. Biopotential monitoring has been part of medicine and rehabilitation protocols for decades now, thus its integration within wearable systems is a natural progression, however a number of factors can affect acquisition reliability such as, electrode-skin impedance fluctuations and data-acquisition circuits' malfunction. This article presents a built-in self-testing approach for an EMG unit, part of a wearable gait monitoring system. The approach utilizes a mixed-signal test infrastructure managed through a dual purpose digital bus, which serves for communication (I2C) and stimuli propagation.**

Keywords - BIST; EMG module; electrode-skin impedance; sigma-delta; I2C.

I. INTRODUCTION

Until recently, most research involving the capture and analysis of biometric and physiological signals has been limited to a laboratory or otherwise controlled environment, making use of cumbersome and costly equipment, which requires specialized facilities and trained personnel. Such research, although useful in its own right, fails to consider real life scenarios and their impact on the subject. The fast paced developments of body sensor networks (BSN) and wearable technologies (including the so called smart textiles) allowed for the next stage in human behaviour analysis tools, and introduces a new understanding of the interaction of individuals with their surrounding environment [1].

Although, wearable and portable biomedical monitoring devices are rapidly becoming a recognized alternative, little attention has been paid to field testing protocols in order to insure measurement reliability, especially when considering long-term scenarios. Testing and design for testability (DfT) have become a crucial aspect of most electronic designs, moreover considering the structural complexities involved in modern packaging technologies.

During biological signals capture, modules' faults (either catastrophic or parametric) can occur in both sensors and signal conditioning circuitry (SCC). This is even more acute when these modules are integrated within wearable systems, due to the harsh conditions they are subject to. In order to improve wearable systems reliability, built-in testing and calibration functionalities are required, which permit faults detection and diagnosis prior data is erroneously captured.

Although significant advances in the last decades have been made on the development and use of standard test infrastructures for digital circuits, such is not the case for analogue or mixed signal scenarios, in spite of the availability of the IEEE 1149.4 test bus [2] [3]. Nevertheless, a number of *ad hoc* contributions and strategies exist, where the general idea is the evaluation of an analog response to controlled stimuli, in order to verify expected response behavior and correlating deviations to specific faults in certain cases [4] [5].

In contrast, the electrode-skin interface, as well as its effect on biosignals measurements, has been well studied [6] [7] [8]. A number of strategies exist for the electrode-skin impedance characterization [9] [10], but the introduction of new electrodes types (textile and capacitive for example) present novel challenges, especially in the case of electromyographic (EMG) signals acquisition [11]. The traditional approach for insuring quality electrode based bioelectric monitoring is through a thorough skin preparation of the target area, verified with a portable skin-impedance meter or utilizing a test signal of the acquisition system. Methods such as the ones presented in [12] [13] provide a continuos monitoring of electrode-skin interface through the inclusion of additional hardware such as signal generators, current sources, filters, used in parallel with the target signal acquisition components.

This article presents a BIST solution for an EMG module of a wearable system intended for gait analysis. The strategy focuses on resource reutilization and component count minimization, through the reuse of an inter-integrated circuit (I2C) bus as a stimuli/response transport, managed through a novel protocol. Section 2 provides an overview of the wearable acquisition system for gait analysis design on which the present work was based. Section 3 presents the BIST strategies implemented, as well as the management framework. Section 4 summarized the experimental test results, and section 5 states the conclusions of the work.
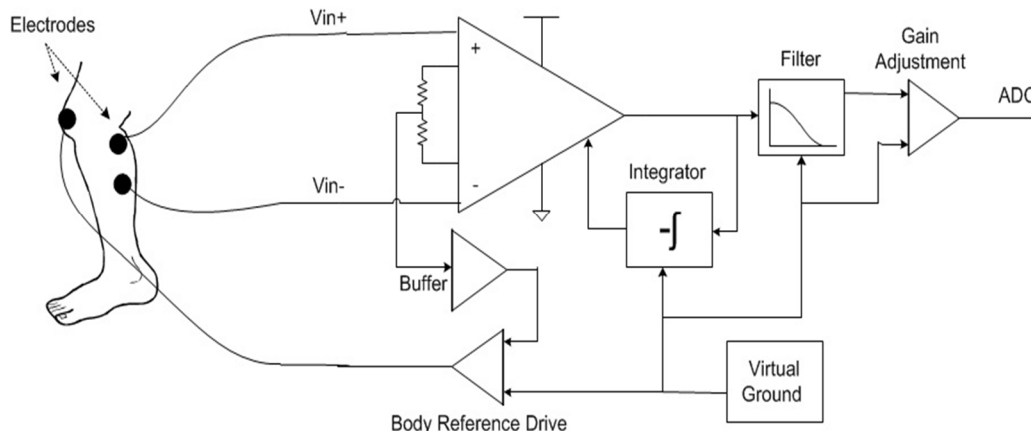
Figure 1. EMG signal conditioning module structure.

II. WEARABLE DATA ACQUISITION SYSTEM FOR GAIT ANALYSIS

Current instrumentation and methods for gait analysis are still expensive and complex, difficult to setup by healthcare staff, hard to operate and uncomfortable for the patient, while requiring a very high level of expertise for data gathering, analysis and interpretation. A new instrument infrastructure specifically dedicated to capturing locomotion data is being developed [14]. The objective is to produce a patient friendly product, capable of providing reliable data for clinicians. It consists of a legwear with customized textile-embedded sensing electronic devices, interconnected by a wired body sensor network that captures inertial and EMG signals, which sends aggregated information to a personal computer through a wireless link.

A. EMG Module

The EMG module contained within each sensor node, shown in Figure 1, can be divided in two main sections: the electrodes and the signal conditioning circuitry. The electrodes are sewn directly on the fabric using conductive yarns made of a polymeric filament covered by a very thin layer of silver, and grouped in sets of two acquisition electrodes and a reference electrode. The SCC comprises the following stages: a differential amplifier, drift removal, filtering, gain adjustment, and a body reference drive feedback. These stages have a predictable behavior established by their configuration and/or combination of elements such as resistors and capacitors, which show an acceptable dispersion of values among them, maintaining the proper functioning of the system. However, variations in the components' manufacturing process, different life-time degradations, electrical faults (shorts and open circuits), or environmental issues such as, humidity, pressure or temperature, can alter such balance of values. Therefore, it is important to ensure that the system is operating within the defined limits before and during its usage, in order to insure the reliability of the captured data.

III. BUILT-IN SELF-TESTING

Built-in self-testing/calibration (BISTC) strategies have traditionally focused on performing detection, diagnosis and repair actions of a specific module, section, component, or IP core [15] [16]. The increasing complexity of modern wearable monitoring technology (WMT) can seldom benefit from strategies that are either too centralized, external data/equipment dependent, or component focused. Communication overhead, increased complexity and resources, or energy expenditure, are just a few factors that limit traditional approaches.

In order to address some of the before mentioned limitations, a BISTC method was proposed, which reduces implementation overhead through the reuse of the I2C bus for testing management purposes, all within a proprietary I2C compliant testing framework named SCPS (setup, capture, process and scan) [17]; making use of the already existing I2C bus for communication purposes, resource management and stimuli-response propagation. Figure 2 illustrates an overview of the infrastructure when applied in an embedded electrodes test instrument.
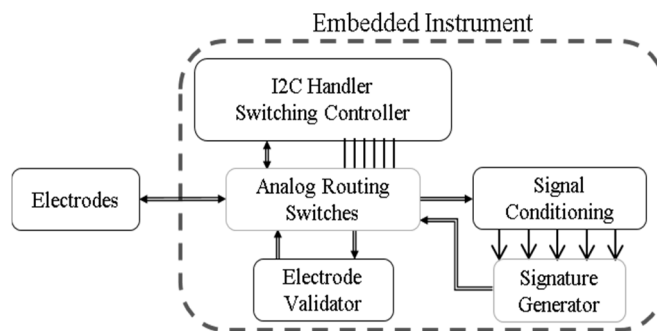

Figure 2. EMG module BISTC structure.

A. Electrode-skin Verification

Electrodes are probably the most widely used sensors for capturing different biosignals within WMT. The contact impedance achieved in the electrode-skin interface affects

biosignals measurements (as stated earlier), a matter of concern, traditionally resolved through, namely, skin preparation procedures, equipment checking, and electrode replacement. Even under such controlled conditions, variations of the electrode-skin contact impedance are to be expected. However, in most of the applications, such as athlete's performance and daily activities monitoring, or other scenarios where the individuals will have to position the electrodes themselves or the electrodes are integrated within a garment, careful positioning and skin preparation cannot be guaranteed.

In the case of textile electrodes the problems are exacerbated, due to their sensitivity to pressure, fabric stretching, and motion artifacts [18] [19]. In addition, textile electrodes and wires (Figure 3) are relatively new technologies and strong behavioral models have not been well established (when compared to pre-gel electrodes).
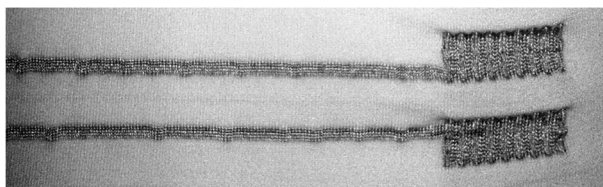
Figure 3. Embedded textile EMG electrodes.

A simple electrode-skin impedance verification circuit was developed following a straight forward approach, by injection of a small current in order to ascertain an electrode pair target load. Individual electrode-skin interface strategies generally utilize a three electrodes approach (one electrode-skin contact target and two others for sinking and voltage reference respectively); however, an electrode pair-wise verification was preferred in this case, in order to maintain approach simplicity. A single supply current to voltage converter is used (Figure 4), which includes a calibration resistor in parallel with the target load in order to control threshold limits and avoid open feedback scenarios. The stimulating current being introduced to the body is a paramount consideration, in order to comply with IEC60601-1 standards, thus the presence of a limiting reference resistor. A local DC reference can be applied as stimulus, in addition to a virtual ground compensated square wave signal sent through the I2C bus.

B. Signal condition circuitry verification

Common-mode rejection, amplification and filtering are regular stages of any electrode based signal conditioning circuit [20]. Such conditioning is performed in order to reduce the effects of common-mode potentials, random noise, motion and power-line artifacts, as well as to effectively retrieving the components of interest of the measured signal. Amplification factors and cut-off frequencies are dependent on the signal type [20], and deviation can cause unwanted elements to be introduced into the conditioned signal.
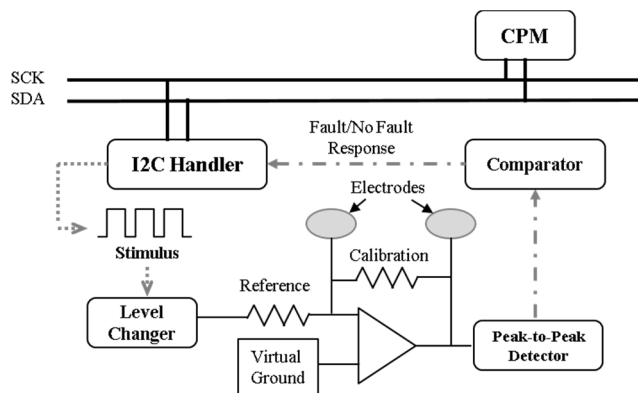

Figure 4. Electrode-skin verification structure.

The test of the SCC is achieved by means of the injection of a square stimulus at the input and the collection of its response in the form of a digital signature that can be compared to a pre-determined golden response. This response actually consists of a set of signatures corresponding to the tolerance determined by acceptable components variations. Initially a Built-In Logic Block Observer (BILBO)-like [21] based approach was attempted in which the stimulus was provided by an LFSR (Linear Feedback Shift Register), and the response of the SCC was collected by a Multiple Input Signature Register (MISR). However, such solution proved to be ineffective, since large variations of some components of the SCC module rendered signatures not so different from those considered valid values, thus providing unreliable and ambiguous error detecting methods for this specific purpose.
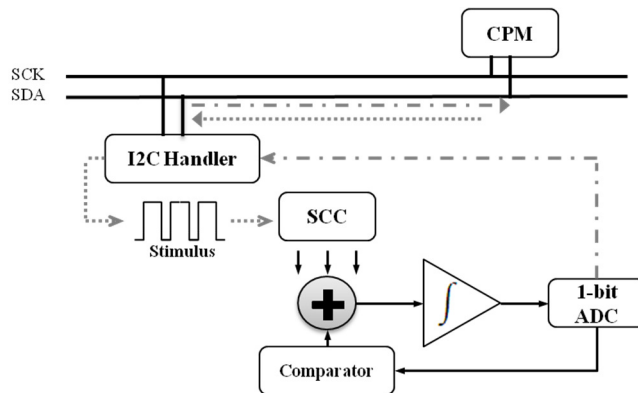

Figure 5. SCC test infrastructure.

Alternatively, a different testing approach was attempted, relying on the I2C Bus for stimuli generation and response capture purposes (Figure 5). An I2C Bus driven stimulus was preferred over a locally generated one, in order to reduce local sources of noise (such as clocks), gain increased stimulus shaped flexibility, and reuse of existing resources. The SCC is tested after capturing its transient response to an impulse designed in order to stimulate the

SCC frequency bandwidth and amplitude full range. This transient, as well as that observed in another internal node of the SCC are then converted to a single digital bit stream by means of a delta-sigma modulator. The observation of different analog nodes and their compression in a single bit stream improves observability and saves test response resources and time. This way the need for an analog test bus line, the inclusion of a complex analogue to digital converter and the multiplexing test response acquisition are avoided.

In order to reduce noise along the communication lines, complexity and total area of the test circuit, it was decided to differ from traditional delta-sigma modulators, by eliminating the flip-flops generally present between comparators. The resulting signature is transported through the I2C lines to a local processing module, which applies a Ziv-Lempel based lossless compression algorithm [22]. This algorithm replaces repetitive bit sequences by a shorter code, as described in the following pseudo-code:

$$array = \Sigma\Delta \ output$$
$$foreach \ segment \ from \ array$$
$$if \ segment \ \in dictionary$$
$$then \ signature \ + = segment$$
$$foreach \ segment \ from \ signature$$
$$if \ segment \ \in 2nd \ dictionary$$
$$then \ final \ signature \ += segment$$

Figure 6. Pseudo-code for compression algorithm.

The use of this compression algorithm is twofold. In the one hand, compression allows reducing the length of data to be transmitted along the wired network from the sensor node to the central processing module (CPM), thus reducing communication time and power, and on the other hand it permits for the analog response external recovery, using the corresponding decompressing algorithm.

C. SCPS and the I2C Handler

A testing and/or calibration strategy for WMT benefits from a group or multi-sensor approach. Such approach could seek to maintain data reliability through recognition of deviating degradation patterns on sensors that could provide insight into system problems due to improper sensor positioning, induced electrical effects due to movement (turboelectric and piezoelectric effects), structural flaws and other factors that require the coverage provided by a group and/or multi-sensor approach. In order to manage the previously mentioned approach a testing framework was designed based on a protocol named SCPS. The SCPS protocol seeks to standardize the command sequence for sensor acquisition/testing access. An I2C based implementation was designed with broadcast, multicast and unicast commands set in order to address modules as groups.

In the present case the command set is utilized for routing elements configuration, and in the case of on-the-fly stimuli configurability, a sequence compatible with I2C

communication is used for transporting stimuli and responses to and from the target module as described in Figure 7.
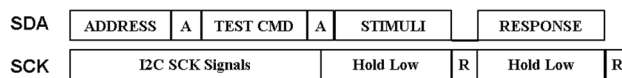

Figure 7. I2C compatible sequence for Stimulus/Response transport.

The sequence sets up the appropriate routing configuration through acknowledgement of a test command and uses the next two SCK low from stimulus and response transport. In order to avoid start/stop events from occurring, the master element insures a low state of the SDA prior to SCK high. A re-start or stop event can then be used at the event of the sequence to finalize the action.

IV. RESULTS

The electrode verification circuit was simulated on Multisim 11.0.775 with database version 11.0.b. Preliminary experiments were performed on an Agar based gel for performance verification prior to testing on human volunteers. A number of signals were used for behavior confirmation, as can be seen in Figure 8, Figure 9, and Figure 10.
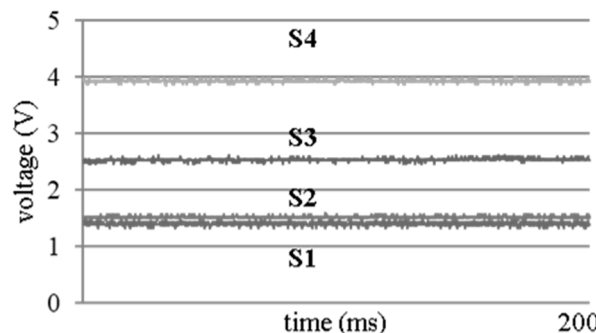

Figure 8. DC Stimuli response for varying conditions, where S1 is the stimuli, S2 is low impedance response, S3 is an expected impedance response and S4 is a high impedance response.
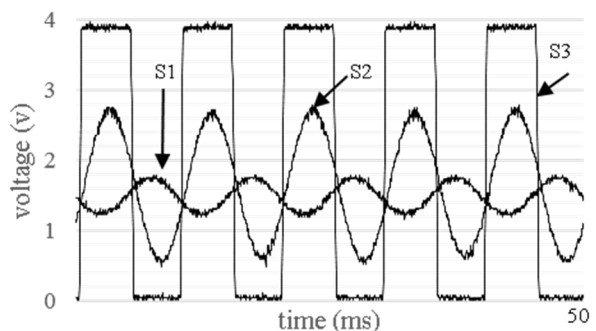

Figure 9. Sine wave of 100 Hz stimuli response for varying conditions, where S1 is the stimuli, S2 is a normal impedance response and S3 is a high impedance response.

The electrode-skin impedance was controlled through variations of the contact surface between the electrode and the skin. Figure 8 presents the behaviour response of the

circuit to such variations for a 10 µA DC stimulus, proving its compatibility with a threshold fault determination approach. Figure 9 and Figure 10 present corresponding responses to a sinewave and squarewave stimuli of matching peak to peak amplitude, respectively (limited to 50 µA). Such responses reveal their sensitivity to the reactive component of the electrode-skin impedance (through phase and time response effects).
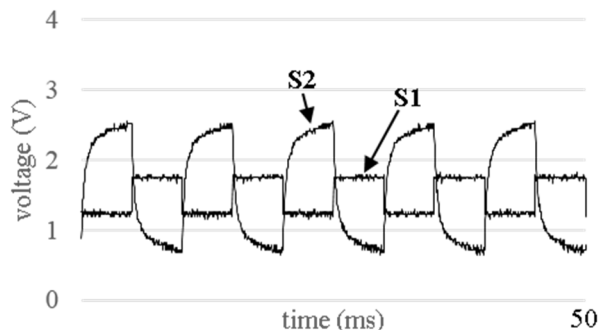

Figure 10. Square wave of 100 Hz stimuli, where S1 is the stimuli, and S2 is an expected impedance response.

A. Signature generation results

The SCC and the delta-sigma circuits were simulated within a SPICE like simulator, using manufacturers' models for the operational amplifiers, comparators and analog switches. Figures 11 to 14 show the waveforms obtained in response to an impulse, for golden and faulty cases. The input pulse stimulus was designed considering the circuit time constants and the I2C time specifications – I2C's fast-mode and fast-mode plus specifications impose minimum durations of 0.6 and 0.26 µs high periods, respectively [23].
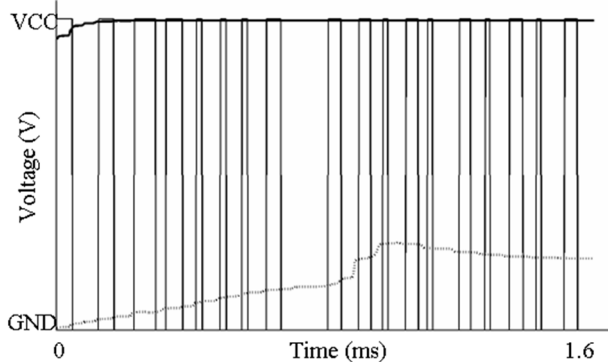
Figure 11. SCC golden response; SCC output (—), internal node (…), sigma-delta output (pulses).

Figures 12, 13 and 14 present faulty responses in the cases of, respectively: a 5% reduction of the filter's gain, a 30% reduction of the low-pass filter's capacitor, and an open connection at the instrumentation amplifier's gain. The sequences of pulses presented in each case are the corresponding outputs of the delta-sigma modulator. It can be seen that, after comparing these sequences with the golden case, the three faults are detectable. The comparison is actually done after capturing them with the I2C controlled infrastructure. This direct capture is possible because the

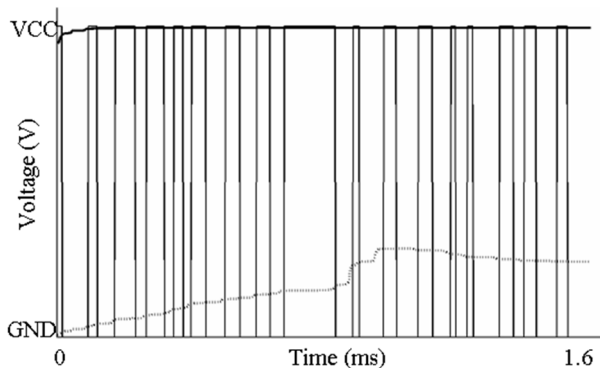I2C sampling frequency allows doing it with an adequate resolution, i.e., no pulses are lost.

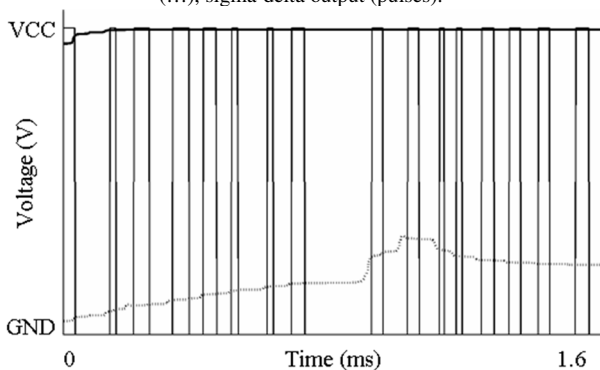Figure 12. 5% reduction of filter's gain; SCC output (—), internal node (…), sigma-delta output (pulses).

Figure 13. 30% reduction of low-pass-filter´s capacitor; SCC output (—), internal node (…), sigma-delta output (pulses).
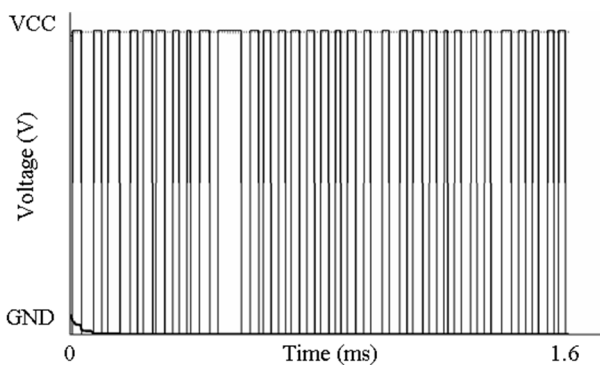

Figure 14. Open connection in instrumentation amplifier's output; SCC output (—), internal node (…), sigma-delta output (pulses).

The bit-stream that is then obtained presents duration of 1.4 ms, or a length of 140 bits. The Ziv-Lempel compression implemented in the local processing unit allows reducing this length in order to transmit a shorter number of bits.

V. CONCLUSION

A mixed-signal built-in self-test infrastructure and methodology is presented that covers the need to address the in-situ verification of the electrode-skin interface, as well as

the functional response of the associated signal conditioning circuitry, for a EMG module of a wearable data acquisition system for gait analysis purposes. The approach being proposed uses an I2C bus for test event management, as well as, stimuli/response transport through a protocol meant for resource optimization and sensor group testing strategies. The electrode-skin interface is evaluated after the measure of the differential impedance and the signal conditioning circuitry is tested after comparing its pulse response with the expected golden response. A Ziv-Lempel compression algorithm is used to allow transferring a shorter version of the captured bit stream, thus saving communication time and power, while preserving the possibility of reconstructing the circuit's pulse response. The simulations and circuit implementation results confirm the validation of the approaches being proposed and reveal their compatibility to the target system and available resources. Significance

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TICE.Healthy Framework for Developing an Ecosystem of Applications in the Domain of Informal Health

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Abstract— **This paper presents a platform being developed in a large scale national project that aims to create an ecosystem of services and applications where patients, relatives and healthcare professionals can cooperate in day-to-day activities. It will implement functionalities for managing medical, social and context information, for integrating mobile devices, remote control and sensors, with insurance of information security.**

Keywords-eHealth; informal healthcare; service-oriented architecture; REST.

I.   INTRODUCTION

TICE.Healthy – Health and Quality of Life Systems – is a research and development project that represents a collaborative effort to design and deploy innovative products and applications in the fields of eHealth and Ageing-Well. The main goal of this project is to create a web-based platform, named eVida, designed to ensure a set of services/features to support the creation of new products, processes, services and applications [1], [2].

From a global perspective, the platform being developed plays the central role within the project TICE.Healthy. Its primary objectives are data acquisition and processing from various collaborating entities (data providers – supply side) so that it can be shared and used by service providers. The eVida website can be consulted at [3], and a promotional video demonstrating some of its features is available at [4].

It is true that we are now witnessing a proliferation of eHealth platforms [5]; however, they are mainly focused on offering a single service. eVida's innovation comes precisely from breaking free of this paradigm by allowing the creation of an ecosystem of applications that can provide complementing capabilities and whose value can potentially supersede the sum of the benefits delivered by each individual application.

This paper presents the architectural approach and a brief description of the main modules comprising the eVida platform.

The paper is organized as follows. Section II presents an analysis of related work. Section III gives an overview of the platform's architecture. Section IV presents the main modules that make up the platform. Section V describes the Web Portal, more specifically: its purpose, the main features

it provides for developers, the types of applications that are supported in the marketplace and a high-level view of its architecture. Section VI provides conclusions for this paper.

II.   STATE OF THE ART

This section analyses current market solutions that present comparable functionalities to the ones required by the eVida platform. Although this analysis includes eHealth platforms it does not focus exclusively on that use case.

A.   Commercial Web Portals

Google Health has been permanently discontinued since it did not reach the initially expected product adoption. However, it is still relevant since it was one of the primary commercial platforms available providing personal health records. This platform allowed users to persist, manage and share the user's health data with other users. It also provided an API allowing the users to share data with external applications that could provide several services like scheduling appointments, processing health data, among others [6].

Microsoft HealthVault is an XML-over-HTTP web service exposing a set of XML-based methods that developers can leverage to build applications that connect to HealthVault. Also, a number of SDKs are available that deliver platform-specific abstractions for working with HealthVault [7]. It is worth noting that this platform is only available in the United States of America and the United Kingdom. Although Microsoft Health Vault supports an ecosystem of other platforms and partner services to leverage the user's data, assuming the required permissions over the data were granted, it lacks many important features. Specifically, this platform does not integrate web applications in a single place and it does not provide the final user with a transparent and singular experience while using the platform. In other words, HealthVault does not support embedded applications, meaning each application runs independently, outside of HealthVault and no mechanisms are provided for inter-app communication. Furthermore, it does not provide Single-Sign-On [8], which is a facility through which a user logs in once and gains access to all systems without being prompted to log in again at each of them. In fact, in order to start using a new application the user is taken to the service provider's website where he

needs to register, sign-in and link the new account to the HealthVault account.

iGoogle is a service provided by Google that consists of a web portal that supports web feeds and web gadgets. The gadgets are defined through an open custom specification called Google Gadgets [9]. Both the development and use of the applications is open to the public [10]. It works similarly to other portals such as My Yahoo!, Netvibes and Pageflakes [11].

Facebook Apps consist of applications hosted in an external server that are accessed in Facebook in a page called Canvas. Together, they provide functionality through APIs, such as the Social Channels API that includes bookmarks, notifications, News Feed stories and search [12]. Facebook also offers an authentication system, called Facebook Connect, as an alternative mechanism to the registration of a user. In other words, Facebook Connect allows external applications to support Facebook accounts [13].

LinkedIn supports applications that follow the OpenSocial specification [14]. These applications can be added to the user's homepage and to his personal profile [15].

Twitter does not support applications in the same way as the previous examples. It offers a REST API that enables third-party applications to interact with the majority of the web site's functionalities [16]. It also provides an authorization and authentication mechanism that can be used by external applications (similarly to Facebook Connect). To that end, Twitter employs OAuth. The permissions that a user can grant are granular enough that he can limit the access to specific data and communication on his behalf.

Chrome Web Store allows the specification of applications published as a compressed archive composed of a manifest, HTML, CSS, and JavaScript files [17] or as a pointer to an external server [18]. Neither type of application is embedded in the Chrome Web Store. Also, the mechanism for executing the applications is not interoperable; it's restricted to the Chrome browser.

Podio is a web system that supports collaborative work for companies and provides extensibility through external web applications. It allows the discovery and purchase of applications similarly to the Chrome Web Store [19].

Table I presents a comparison of the functionalities of the various commercial projects that were presented.

TABLE I.   COMPARISON OF THE FUNCTIONALITIES OF THE COMMERCIAL PROJECTS THAT WERE ANALYSED

	Embedded apps	Single sign-on	Granular Permissions	Consistent UI	Cross-browser	Supports web apps	Supports native mobile apps
Google Health	✗	✗	✗	✗	✓	✓	✓
Health Vault	✗	✗	✓	✗	✓	✓	✓
iGoogle	✓	✓	✗	✗	✓	✓	✗
Facebook Apps	✓	✓	✓	✓	✓	✓	✓
LinkedIn Apps	✓	✓	✓	✓	✓	✓	✗
Twitter Apps	✗	✓	✓	✗	✓	✓	✓
Chrome Web Store	✗	✗	✓	✗	✗	✓	✗
Podio App Store	✓	✓	✗	✓	✓	✓	✓
eVida	✓	✓	✓	✓	✓	✓	✓

eVida already supports the most common features provided by major web portals. However, it is an ongoing project with many required functionalities still in development, such as a payment system for the marketplace and a fully featured interoperability module.

III.   PLATFORM ARCHITECTURE OVERVIEW

The platform's architecture is based on the design principles of service-oriented architectures (SOA), because of its distributed and extensible nature. This approach increases the abstraction and encapsulation within the system. The platform exposes a set of Representational State Transfer (REST) services as the communication mechanism with the data and service providers. Fig. 1 illustrates the high-level architecture of the platform. Three main components can be easily identified, which implement the information and interaction channels for selling products and health services: the database stores all the administrative data, and configuration data of the platform; the backend services provide security, interoperability and information services; and the frontend is comprised by the platform's web portal, which exposes the tools to submit and publish applications within the platform's ecosystem.
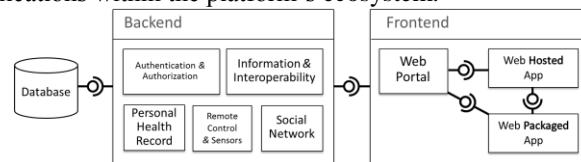

Figure 1.   The platform's high-level architecture.

This platform implements functionalities to manage medical, social and context information, for integrating mobile devices, remote control and sensors, with insurance of information security.

IV.   PLATFORM MODULES

This section will briefly present the modules that make up the platform.

A. Mobile Devices, Remote Control and Sensors

The purpose of this module is to simplify the development and integration of new and innovative services for the provision of health care and communication. This kind of services is often referred to as home care in assisted environments and domotics (e.g., measuring biometric signals and leveraging environmental sensors). This module is also responsible for accessing services deployed in eVida with mobile devices, following the technological trends of accessing Internet services through smartphones and tablets.

The platform includes mechanisms for collecting and transmitting data in real-time. For this purpose it provides a Jabber/Extensible Messaging and Presence Protocol (XMPP) [20] interface for gathering and sharing data on a continuous basis. An example of usage of this infrastructure is the real-time acquisition of sensor data.

B. Security

The security module aims to ensure that applications and services that work on the platform are reliable in terms of confidentiality, integrity and availability of information. These three aspects are essential to ensure an acceptable level of security and privacy of the user's personal information and data stored in the platform. This module's components will cover all logical layers of the platform, from the access control of users and systems, to the use of encryption in network protocols. Specifically, this module will be responsible for the *authentication* – by verifying the identity of the applications that interact with the platform using the OAuth 1.0 or OAuth 2.0 protocol (eVida provides both) – and *authorization* – by verifying data access permissions.

The *permissions* module that was developed is flexible due to the dynamic nature of our health data repository. In the current integration it allows platform administrators to:

- Create roles with (Create, Read, Update and Delete) permissions over archetypes, records and the personal health record viewer application's menus.
- Define permissions directly associated with users and associate them with roles.

In the personal health data viewer application the user can:

- Create and manage groups to whom he associates permissions and users.
- Access other users' personal health data with proper authorization, limited to the permissions provided by his roles and by the groups to which the data owner has associated him with.

We chose to distinguish between role and group (this concepts are not consistent across the literature [21]) and implement both. In our system groups are a convenient method for users to associate a name to a set of subjects and permissions and use this name for access control. On the other hand, roles are defined at the system level, by the platform managers, as a collection of privileges required to perform specific actions in the system.

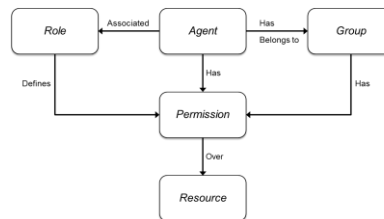The logical diagram of the permissions module is presented in Fig. 2.

Figure 2.   Logical diagram of the permissions module.

An agent can have several permissions over the same resource defined in different ways. For example, he can be associated to a profile and be part of a group that both define permissions over the resource.

The permissions are defined as capabilities [22]. A capability consists of an object the user must have in order to execute a specific action over a resource. Each capability has a resource id and operations a user can execute over a resource. Fig. 3 illustrates this concept.
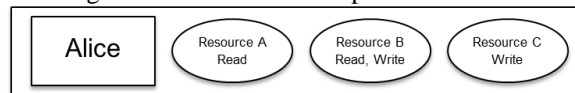

Figure 3.   Conceptual representation of the use of capabilities in the permissions module.

Alice can execute a Read operation over resource A, but she cannot execute a write operation over the same resource. To perform this validation the module uses binary masks, the same mechanism used by the Unix file system [23]. This technique consists of assigning a sequential number that is a power of 2 to each type of action (permission). This way, the set of permissions a user has over a resource is given by the sum of all individual permissions. For example, if we assign the following numbers to the actions:

- Read: 1 (2^0)
- Write: 2 (2^1)
- Edit: 4 (2^2)

If an agent has Read and Write permissions over a resource, then the set of permissions is given by the disjunction of all the individual permissions (1):

$$set = value(Read) \text{ OR } value(Write) = 3 \qquad (1)$$

This technique enables efficient validations, since they become basic logic operations like the one presented above. It is also memory efficient, given that it only requires a 64 bits Long to store all the permissions a user has over a resource.

C. Information and Interoperability

The information and interoperability module facilitates the presentation of information to a large number of services that wish to receive it in a particular format. Specifically, there will be a medical information component, designed to work with the Health Level 7 (HL7) versions 2.x and 3.0 and Digital Imaging and Communications in Medicine (DICOM) standards to provide a comprehensive solution to

the needs of professional caregivers and a connection to other legacy information systems. The components comprising this module allow the development of new services and products that can communicate using the same syntax and semantics.

D. Personal Health Record

A Personal Health Record is a repository of clinical information of an individual whose maintenance and updating can be performed by himself or by his caregivers [5]. This module is responsible for storing the platform's clinical data, which is made available through a REST application programming interface (API). It also presents a user interface where personal health data can be consulted in a secure and private manner. The users will be able to share parts of this data with family, friends, caregivers and service providers.

The PHR is created over an application builder [24] that was designed under the TICE.Healthy initiative. Using this component it is possible to create related business/clinical entities, design forms and views and deploy it as a full application that can be dynamically extended and changed without the need for a redeploy.

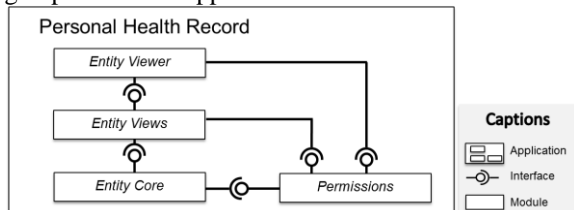Fig. 4 presents the application builder and the PHR.

Figure 4.   Static diagram of the Personal Health Record's Modules.

Fig. 4 presents four modules that serve as a foundation for the PHR application:

- The permissions module, that was previously presented, handles the system's authorization.
- The Entity Core is the layer that handles the configurable clinical data repository. It provides an internal API with business logic that enables abstraction from the dynamic nature of the data structure. It also provides a REST API for data manipulation.
- Entity Views is responsible for interpreting the configuration of templates and entities/archetypes in order to generate interface elements. It uses Entity Core to manipulate the data and the Permissions Module to check authorizations for data manipulation.
- Entity Viewer presents a dynamic application (the PHR viewer) that can be configured through an administration panel. This high-level module uses the previously described modules, allowing platform administrators to create and manage entities and templates, create application menus, define their content and manage permissions.

V. WEB PORTAL

The platform's frontend includes a marketplace for applications developed by third parties (including applications developed under the scope of TICE.Healthy).

This Web Portal aggregates and integrates applications and offers the final user a unified interface. Currently, the platform provides mechanisms so:

- Developers can add and manage applications in the platform.
- End users can use these applications in the platform without the need to register and sign-in to each of the applications, through a Single-Sign-On mechanism.
- Applications can make use of the platform's REST API and user data, given the necessary permissions.
- Applications can make use of the JavaScript APIs for interacting with the portal, other applications and users.

Furthermore, the platform allows the publication of web applications that can take one of two formats: packaged apps and hosted apps. In addition to the web applications, the marketplace also offers support for mobile applications.

A. Packaged Apps

These applications execute entirely in the browser and their business logic is programmed in JavaScript. They can also make use of the new capabilities of browsers related to HyperText Markup Language 5 (HTML5), such as working in offline mode. These packaged applications consist of an archive that follows the World Wide Web Consortium (W3C) widgets specification. With this specification W3C intends to standardize the way client-side web applications are written, digitally signed, protected, compacted and deployed independently of the platform [25].

Both the portal's API and the web interface communicate with a widgets server. Because the definition of the packaged applications follows an open standard it was possible to choose an open-source implementation to manage them. Apache Wookie [26] was selected for that purpose.

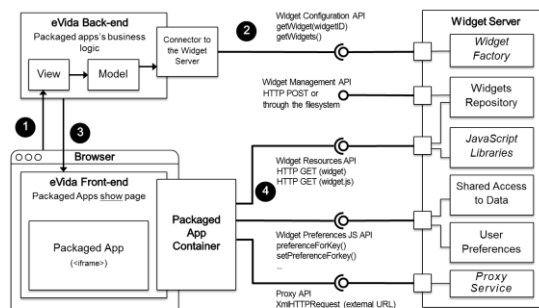The execution process of packaged apps is described in Fig. 5.

Figure 5.   The execution process of packaged apps.

When accessing a packaged app (1) the corresponding view is executed which, in turn, will communicate through the model with the widgets server. The widgets server instantiates the widget and returns the application's URL. At that moment it is possible to present it to the user (3). While

it is being loaded, the resources required for the use of the JavaScript APIs are fetched (4).

Although most packaged applications are highly responsive, fast and interactive, they force the use of a particular programming model which might not always be adequate or desirable. In fact, programming the application entirely in JavaScript can be restrictive in certain contexts. To overcome this constraints the platform also supports hosted applications.

B. Hosted Apps

This type of application is remotely accessible and housed outside of the platform, being supported by its own servers.

Among the choices available for including hosted applications (such as inline JavaScript, content obtained through asynchronous JavaScript and XML – AJAX calls, iframes and script tags), we adopted the use of iframes with additional capabilities, which allow the URL of the portal to be updated as the user navigates in the application and make the application sensitive to events, such as resizing the screen and personalized messages. Also, the applications' content is downloaded asynchronously, thus not affecting the rendering of the portal page.

C. Comparison Between Hosted and Packaged Apps

Table II presents a comparison of the main characteristics of the formats that have been described.

TABLE II.   COMPARISON BEWTEEN HOSTED AND PACKAGED
APPLICATIONS

Criteria	Hosted App	Packaged App
Hosting	Responsibility of the developer	In the platform
Technological paradigm	Any language and technology	JavaScript executed in the browser
Server	Mandatory	Optional
Communication with the portal and other applications	Supported with limitations[a]	Supported
Data persistence	Responsibility of the developer	Supported

The communication is processed in a secure manner in recent browsers, however, the fallback that takes place in older browsers (Internet Explorer $\leqslant$ 7, Mozilla Firefox $\leqslant$ 2.0, Safari $\leqslant$ 3.2, Opera $\leqslant$ 9) is unsafe, so it cannot be used to transmit sensitive data.

It is also worth mentioning that, from the platform's perspective, it is better to have a packaged application since it provides a more seamless integration and, typically, a more responsive feel to its users. In terms of managing the applications it is also easier for administrators to control packaged applications because whenever a developer makes a change he needs to resubmit the application for approval. On the other hand, hosted applications can be changed without going through this process, thus requiring periodical

verifications to make sure they still abide by the platform's terms and policies.

D. Isolated Environments

The portal's domain is different from the domains that serve both the hosted and packaged applications. This adds security since the browsers restrict the interaction between frames in which the domain, port or protocol differ. However, what is gained in security is lost in interaction capabilities. In the case of packaged apps that can execute JavaScript code using shared objects a different solution is required. In those cases, the Google Caja [27] web service is applied, which is a compiler for making third-party HTML, CSS and JavaScript safe for embedding, that follows the Object Capabilities [28] security model. This allows the isolation of the execution of the code so that the application integrated in the portal can only manipulate certain objects.

E. General Objectives of the JavaScript APIs

Each type of application (hosted and packaged) has its own technical specificities and associated scripts to guarantee the correct access to the APIs. In the case of hosted applications, the developer needs to import the script manually.

Presently, the developed APIs are:

- Inter-App Communication – offers mechanisms for communicating through a Publish-Subscribe model. A producer (application) can share data publicly (all users) or privately (across browser sessions of one user). Only private channels require user login. In both the public and private channels if the producer decides to share data he can specify which are the authorized receivers (based on their application IDs) or he can share the data with everyone (any application can become a subscriber). In the public channels the user (who may or may not be logged in) is prompted to authorize or reject the channel when the application tries to perform its registration. In the private channels the user can have his sessions initiated in multiple browsers and devices and he is prompted to authorize or reject the channel the application tries to subscribe.
- Remote Communication & Debugging – set of functions that facilitate the debugging process allowing asynchronous communication with external resources.
- Widget Properties – allows access to the properties that define the application, such as metadata included in the applications configuration file and properties related to the execution of the application in the portal (i.e., the language setting for the user in the portal). This API follows the Widget Interface specification defined by the W3C and is partially implemented by Apache Wookie.
- Widget Extensions – offers methods that extend the abilities of the applications. One of the most important methods allows the application to know if the user is logged in.

- Widget Preferences – supports the manipulation of a data persistence area unique to the application instance. The application can use this to store customizable configurations that are specific to a user. This API follows the Widget Interface specification defined by W3C and is implemented by Apache Wookie.
- Wookie Utilities – Helper functions that enable the dynamic update of the web page with content from external sources like servers or the user's input. This API is implemented by the Direct Web Remoting library [29].

You can learn more about these APIs at [30].

F. Inter-App Communication API

In order to support communication through private channels, a flow was defined that would guarantee the authenticity of the user. Inspired by the way the web Pusher service provides a similar mechanism [31], the following process was defined (Fig. 6):
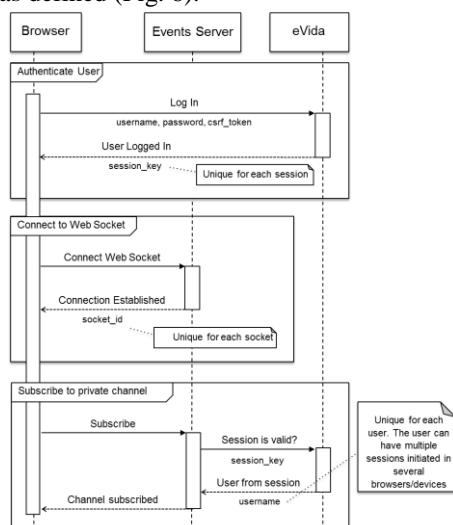

Figure 6. Protection mechanism for private communication channels.

Firstly, the user needs to be authenticated in the portal in order to use the private channels. The user's session key is generated during the login process. As soon as the user executes the first web app, a connection to the events server is established. That connection is uniquely identified by its session id. Afterwards, when a private channel is subscribed, the user's session key allows the identification of the user (provided that the session key is valid).

G. Remote Storage

eVida's users and developers are encouraged to store their data in the platform's repository but are also free to choose other options. To illustrate one alternative to eVida's developers an example packaged app [32], that enables the user to store their data at a place of their choice, was created. This example uses the remoteStorage.js library [33], a client side implementation of the remoteStorage specification [34]. This approach can have several advantages from both the users' and developers' perspectives. From a user's

perspective he can effectively own is data and have everything in one place. He can setup a storage account with a provider he trusts or, ultimately, setup his own storage server and the data will always be with him regardless of his location or the status of the applications he uses (i.e., sometimes companies shutdown their services and users may lose their data). From the developers point of view they can develop their web app without worrying about hosting or even developing a backend since the users will connect their own backend at runtime.

H. High-Level View of the Portal and its Connections With Other Entities

Fig. 7 presents the high-level view of the static perspective of the web portal with the representation of the connections to external entities.
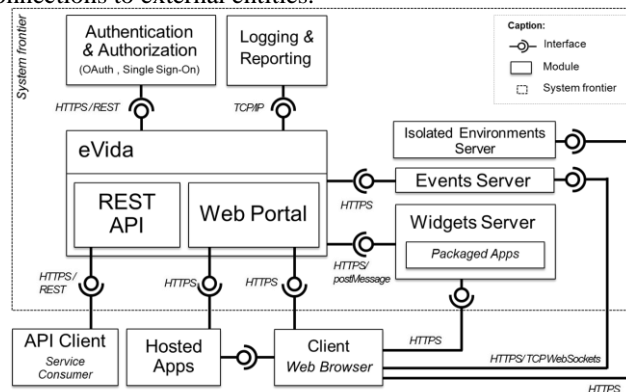

Figure 7. High-level view of the portal's architecure and connections with other modules and external entities.

Note that although the final user only accesses the link to the web interface, in practice, his browser communicates internally in a direct manner with the events, widgets and isolated environment servers, as well as with external applications. The connection established with the events server uses web sockets, or AJAX requests in case web sockets are not supported by the user's browser. The applications communicate with the portal using the postMessage method, which allows the communication between frames of an HTML page through JavaScript (thus not involving network requests).

VI. CONCLUSION

In summary, TICE.Healthy provides the infrastructure and support for an ecosystem of smart and innovative Information and Communications Technology (ICT) services, applications and products for the eHealth and Ageing-Well market. It provisions the developers and the solution providers with basic platform services, such as: authentication and authorization mechanisms, a repository for personal health data, flexible sensor integration and many more. In this manner, TICE.Healthy helps to create an ecosystem of interoperable hardware and software products with greater joint benefit for the end user.

This paper also presented a web portal that operates as information and interaction channel for selling products and

health services. This channel is used to process the exploring of applications and integrate them by allowing them to work around the same context and use common mechanisms. Each user is able to associate his profile with applications provided by the platform, which is responsible for sharing his context and assures a transparent, uniform and consistent user experience.

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Smart Suit® Lite: KEIROKA TechnologyPaper Title

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Abstract—We are developing a passive power assist supporter called Smart Suit Lite. Smart Suit Lite is a compact and lightweight power assist device that utilizes the elastic force of elastic belts. To design the Smart Suit Lite, we developed a motion-based assist method and an extended musculoskeletal model. The motion-based assist method was used to design the arrangements and properties of the elastic belts by utilizing the relation between the target motions and the corresponding muscle forces. To analyze the assistive forces provided by the elastic belts, skin segments that represent the surface of the human body features the extended musculoskeletal model and can reproduce changes in length of the body surface with changes in posture. In this study, we used the developed method to produce the Smart Suit Lite for care workers. Furthermore, through the "trial experiment" in this experiment, we found that wear comfort was strongly correlated with the assistance perceived by the user. Thus, we have improved the Smart Suit Lite from the aspect of wear comfort and verified the enhancement of the assistance provided by the device. In user testing, 90% of the participants reported a decrease in load on the low back during care work.

Keywords-Power Assist; Iomechanics; Human Body Dynamics Mode; KEIROKA Technology; Smart Suit Lite.

I.   INTRODUCTION

In recent years, rapid aging of the population in many developed countries has led to increased demand for care workers. As a consequence, the physical burden placed on care workers by strenuous tasks and heavy workloads has become a severe problem. Minematsu [1] reported that half of care workers experience back problems. The main causes of low back pain, in particular, are overloading and bad posture [2]. In performing lifting tasks during routine duties, care workers tend to bend deeply at the waist, and the load on the low back is great [3]. Therefore, a power assist device for the low back muscles should be effective in not only reducing fatigue but also preventing lumbar disease.

Recently, many power assist devices have been developed. In particular, wearable assist systems have attracted considerable interest. Many of them are
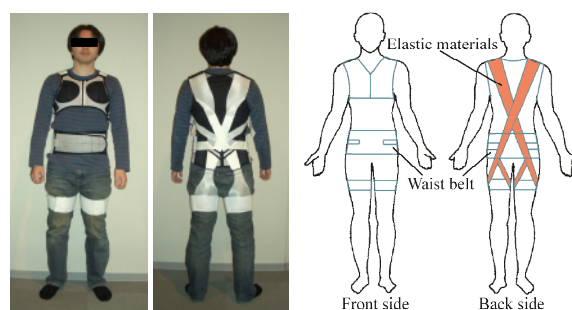
(a) Smart Suit Lite   (b)Form of Elastic belts

Figure 1: Prototype of Smart Suit Lite

exoskeleton-type systems such as HAL [4], Muscle Suit [5] and BLEEX [6]. These exoskeleton suits are able to generate a large assistive force, but are weighty and large, owing to the necessity of both a power source and a number of actuators. On the other hand, some small and light-weight power suits have been developed, for example, Back Muscle Supporter [7], Simple Supporter [8] and Assist Suit [9]. Such devices utilize only passive force, and are designed to reduce the burden placed on the wearer.

In our laboratory, we have been developing a passive power assist supporter Smart Suit Lite (SSL) as one of KEIROKA assistive device. The device utilizes elastic force generated by elastic belts, and thus is safe, easy to use and suitable for nursing care applications. Because SSL does not have a control mechanism, the assistance provided by the system is determined in the design phase. Therefore, this study aims to design elastic belts and optimize the assistance provided for target motions.

Herein, we describe the design method of SSL, and report designs of elastic properties and arrangements of elastic belts for care work. Furthermore, trial experiments were conducted in a hospital and improvements based on the results are reported.
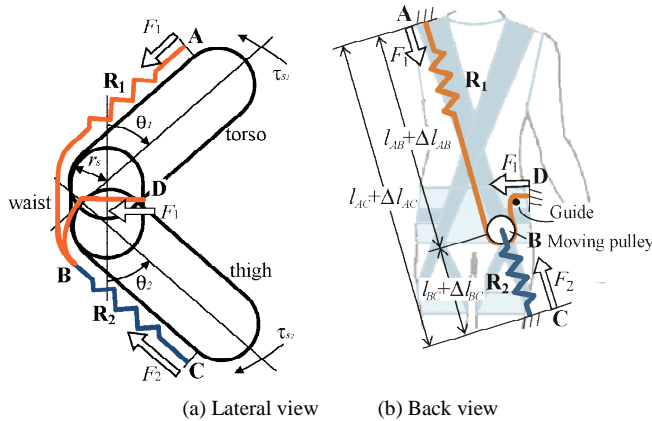
(a) Lateral view   (b) Back view

Figure 2: Assist mechanism of Smart Suit Lite

II.   KEIROKA TECHNOLOGY

KEIROKA is a concept of assistive technologies. It does not only aim to reduce user's fatigue, but also achieve the following:
(1) secure assist for users and surroundings.
(2) sustainable assist to keep user's physical and mental performance.
(3) subliminal assist to keep user's natural motion. Smart suit is one of KEIROKA wearable assist devices designed by the above concepts. This paper describes the design methodology of smart suit lite for nursing workers and its results of field test.

III.   SMART SUIT LITE

Figure 1 shows a prototype of SSL. The elastic belts are arranged to connect the thighs and shoulders to the back, as shown in the figure. Furthermore, SSL is able to fit closely to the wearer's body and the assistive force is set according to the expected workload by adjusting the initial lengths of the elastic belts. Figure 2 shows a schematic side view of the device, and illustrates the assist mechanism in two dimensions; one of the elastic belts is shown. The elastic belt of the upper body R_1 and the elastic belt of the thigh R_2 are connected by a movable pulley at point B. In this configuration, we have belt of the thigh R_2 are connected by a movable pulley at point B. In this configuration, we have

$$F_1 = 2k\Delta l_{AB}, \tag{1}$$

$$F_2 = k\Delta l_{BC}. \tag{2}$$

Here, Δl_{AB} is the change in length between A and B; Δl_{BC} is the change in length between B and C; F_1 and F_2 are the elastic forces provided by R_1 and R_2, respectively; and k is the spring constant.

If $2F_1 = F_2$ and $\Delta l_{AC} = \Delta l_{AB} + \Delta l_{BC}$ where Δl_{AC} is the change in length between A and C, then we have

$$\Delta l_{AB}:\Delta l_{BC} = 1:4. \tag{3}$$

Therefore, assistive torque τ_{s12} is

$$\tau_{s12} = \tau_{s1} + \tau_{s2} = \frac{6}{5}r_s k\Delta l_{AC}. \tag{4}$$

Here, r_s is the moment arm of the elastic belts. Moreover, a part of the elastic force is used as a stabilization force, F_t, at point D. This stabilization forces act on the torso, in the similar manner as a corset.

$$F_t = F_1 = \frac{2}{5}k\Delta l_{AC}. \tag{5}$$

Δl_{AC} increases as the wearer bends forward at the waist, and thus the assistive torque τ_{s12} is higher when adopting a posture that corresponds to higher load on the low back.

IV.   DESIGN OF ELASTIC BELTS USING MOTION-BASED-ASSIST METHOD

A. Algorithm

The motion-based assist method is a design method based on models of the relation between the target motions and muscle forces. In this study, we design the elastic belts of SSL by using this method, which consists of the following steps.

Step1 Determine the sites and motions to be assisted.
Step2 Measure the target motions $\mathbf{M} = [\theta_1 \; \theta_2 \; \cdots \; \theta_N]$ in three dimensions with a motion capture system. Here, N is the number of sampling points; θ_j is posture measured at time $j\Delta t$. (Δt is the sampling period).
Step3 Calculate muscle forces F_h in the target sites and moment arms $\mathbf{r}_h = \{r_{ij}\}$ for each degree of freedom by analyzing the motion $\mathbf{M}$ with a dynamic musculoskeletal model $\mathbf{G}_{SIMM}(\cdot)$. Then, calculate human joint torque τ_h from F_h and $\mathbf{r}_h$.

$$[\mathbf{F}_h, \mathbf{r}_h] = \mathbf{G}_{SIMM}(\mathbf{M}), \tag{6}$$

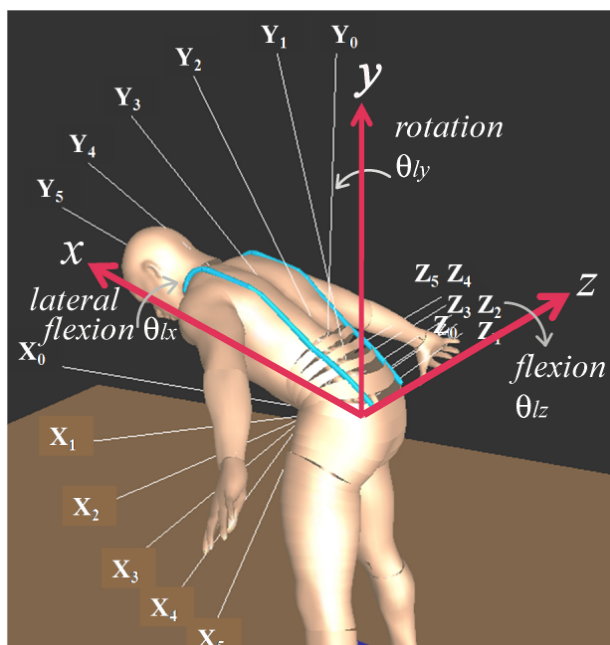$$\tau_h = \mathbf{r}_h \mathbf{F}_h. \tag{7}$$

$$\tag{1}$$

Step4 For arrangement $\mathbf{P}_s$ of the elastic belts, calculate the change in length of the elastic belts (Δl) and the moment arm of the elastic belts ($\mathbf{r}_s$) through analysis using a geometric skin segment model $\mathbf{G}_{SKIN}(\cdot,\cdot)$ and the motion $\mathbf{M}$.
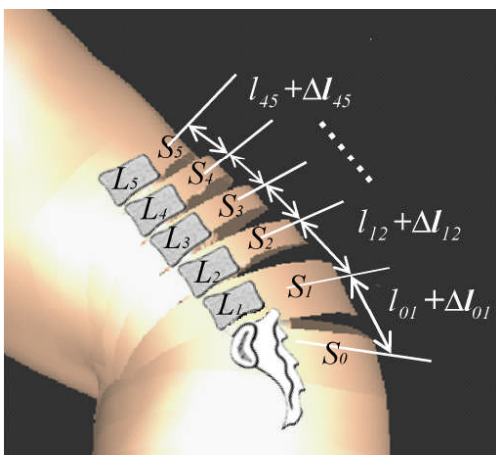
$$[\Delta l, \mathbf{r}_s] = \mathbf{G}_{SKIN}(\mathbf{M}, \mathbf{P}_s). \tag{8}$$

Step5 By repeating Step 4 for each arrangement, find the maximum assistive torque τ_s, and determine the arrangement $\mathbf{P}$. Spring constant k is assumed to be constant in this step.

$$\tau_s = \mathbf{r}_s k \Delta l. \tag{9}$$

(a) Changing patient's posture   (b) Helping patient sit up

(c) Changing patient's location

Figure 4: Caregiving movements to be assisted

Step6 Assuming that the assistance is provided by projection of the assistive torque τ_s to the human joint torque τ h, determine the desired elastic modulus k from Δl and $\mathbf{r}_s$, with desired assistive ratio $\hat{\eta}$.

$$k(j\Delta t) = \hat{\eta} \frac{|\tau_k(j\Delta t)|^2}{\Delta l(j\Delta t)r_k(j\Delta t) - \tau_k(j\Delta t)}, \quad (j = 1, \cdots, N). \tag{10}$$

Step7 Calculate the elastic property curve $\hat{k}(\Delta l)$ from elastic modulus k and the change in length Δl by fitting the data to following expression:

$$\hat{k}(\Delta l) = a_1 \Delta l^{a_2}, \tag{11}$$

where a_1 and a_2 are coefficients of the elastic property.
In this manner, the arrangement and property of the elastic belts are designed.

B. Skin Segment Model

To analyze the assistive force during motions, we developed a skin segment model that represents the body surface as shown in Fig.3 (a). We can calculate the changes in length of the elastic belts along the body surface by modeling the relation between posture and the shape of the body surface. To represent the elongation of skin covering the lumbar area, lumbar segments shown in Fig.3(b) are divided into segments $S_1 - S_5$, which correspond to the lumbar vertebrae ($L_1 - L_5$), and each segments is given coordinates $\Sigma_i (i = 1-5)$. In conjunction with lumbar angle θ_l, which consists of flexion θ_{lz}, lateral flexion θ_{lx} and rotation θ_{ly}, skin segments move with respect to the pelvis at Σ_0 according to the following homogeneous transformation matrix.

(a) Skin segment and coordinate systems

(b) Lumbar segments in flexed posture

Figure 3: Skin segment model

$$\,^{i}\mathbf{T}_{i-1} = \begin{bmatrix} \,^{i}\mathbf{R}_{i-1}(\mathbf{C}_{i}\theta_{i}) & \,^{i}\mathbf{P}_{i-1} \\ \mathbf{0}^{T} & 1 \end{bmatrix} \qquad (12)$$

$$\,^{i}\mathbf{R}_{i-1}(\mathbf{C}_{i}\theta_{i}) = \mathbf{R}_{y}(c_{iy}\theta_{iy})\mathbf{R}_{x}(c_{ix}\theta_{ix})\mathbf{R}_{z}(c_{iz}\theta_{iz}). \quad (13)$$

Here, $\mathbf{R}_{x}$, $\mathbf{R}_{y}$, and $\mathbf{R}_{z}$ are rotation matrices; $\mathbf{C}_{i} = \begin{bmatrix} c_{ix} & c_{iy} & c_{iz} \end{bmatrix}^{T}$ is a coefficient vector; and $\,^{i}\mathbf{P}_{i-1} = \begin{bmatrix} p_{ix} & p_{iy} & p_{iz} \end{bmatrix}^{T}$ is a translation vector. Then, there are gaps between segments as shown in Figure 3 (b). The change in length, Δl, of a path along the body surface is the sum of the change in length between each pair of adjacent segments (i.e., $\Delta l_{(i-1)i}$ ($i = 1 \ldots 5$)).

$$\Delta l = \sum_{i=1}^{5} \Delta l_{(i-1)i} \qquad (14)$$

The size of the skin segments and transformation matrix can be adjusted with parameters, and thus a model can be prepared to suit the wearer.
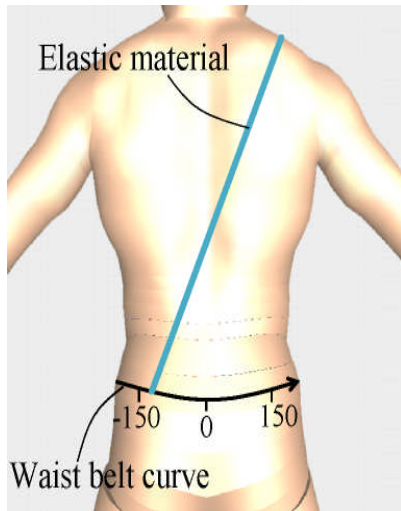

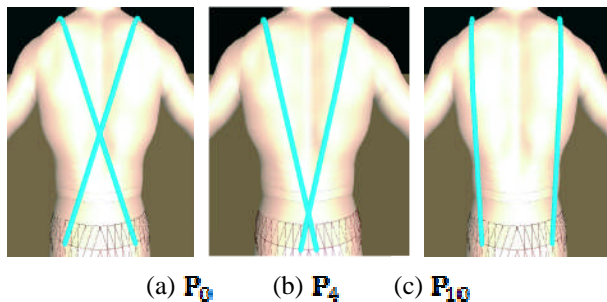Figure 5: Waist belt curve and point of intersection

(a) $\mathbf{P}_{0}$ (b) $\mathbf{P}_{4}$ (c) $\mathbf{P}_{10}$

Figure 6: Arrangements of elastic belts

V. DESIGN OF SMART SUIT LITE FOR CARE WORK

A. Target Motions for Assistance

In this study, common tasks performed around patient's bed in care work were selected as the target motions. Figure 4 shows the selected motions. In preliminary experiment, these tasks were found to place a larger load on lumbar muscles compared with muscles in other regions. We took lumbar muscles to be the main assist target.

B. Design of Elastic Belt Arrangement

In Steps 4 and 5 of the Motion-based assist method, we designed the arrangement of the elastic belts to provide effective assistance to lumbar muscles. Here, design parameters are via points P_{r} and P_{l} on the waist belt curve of the elastic belts (Figure. 5). Via points are symmetrically shifted from -150[mm] to 150[mm] in increments of 30[mm], such that 11 arrangement patterns are defined ($\mathbf{P}_{j}$ ($j = 0, \cdots, 10$)).

$$P_{rj} = -P_{lj} = -150 + 30j \quad (j = 0, \cdots, 10). \qquad (15)$$

Using these arrangements, we performed simulations of assistive torque during the motions of care work. First, motion capture and inverse dynamics analysis were carried out in Step 2 and 3 of the motion-based assist method. Table I shows the conditions of the motion capture experiment. Next, simulations of assistive torque were performed for $k = 500$[N/m]. Below, we define the torque assist ratio as a measure for evaluating the provided assistance.

$$\eta_{\tau} = \frac{1}{T} \int_{0}^{T} \frac{\tau_{s}\tau_{h}}{|\tau_{h}|^{2}} dt. \qquad (16)$$

Here, τ_{s} is assistive torque and τ_{h} is human joint torque.

Selected simulation results are shown in Figure 7. The highest assist rate was found in arrangement $\mathbf{P}_{4}$ (Figure 6). Thus, this arrangement of elastic belts was selected for further investigation.
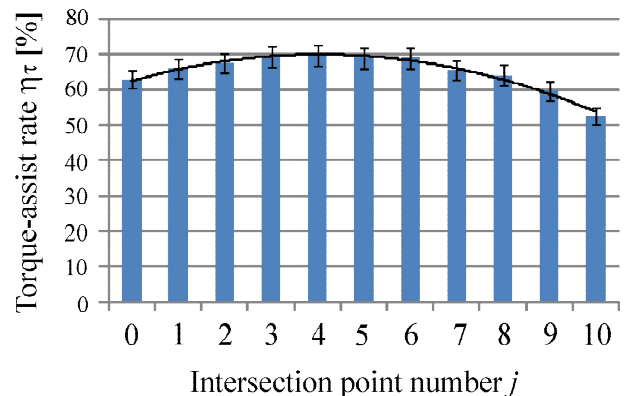

Figure 7: Simulation result for changing patient's posture

TABLE I. CONDITIONS OF MOTION MEASUREMENT

Height of participant	1723 mm
Height of bed	400 mm
Height of patient	1730 mm
Software	EvaRT4.3.57
Cameras	15 (HWAK-200RT)
Force plate	2 (Kistler Inc.)

VI. TRIAL EXPERIMENT

A. Experimental Conditions

To investigate the utility of SSL in the field, we performed a trial experiment at a hospital. Tables II and III show the details of the experiment. Participants wore SSL during working hours for five days and completed a questionnaire each day. Figure 8 shows a representative scene from the trial experiment.

Figure 8: Scene from the trial experiment

TABLE II EXPERIMENT CONDITIONS

Period	July 5 - August 10, 2010
Type of facility	Internal medicine and rehabilitation
Number of participants	20 (caregiving staff members)

TABLE III OVERVIEW OF PARTICIPANTS

Sex	Female	19
	Male	1
Age	30–39	3
	40–49	6
	50–59	11
Lumbar pain	Yes	10
	No	10

B. Results

1. Feeling of fatigue

Participants evaluated fatigue before and after work on the Visual Analog Scale (VAS). The increases in fatigue due to work was compared between work done while wearing SSL and work done while not wearing SSL.

To do this, the increase in VAS for work with SSL was subtracted from the increase in VAS for work without SSL. Table IV shows the results. With respect to the mean for all participants, there is no significant difference in the amount of change in VAS. Next, we divide the participants into groups by comfort while wearing SSL (comfortable, 7; uncomfortable, 13). For the group of participants who feel comfortable while wearing SSL, the amount of change in VAS is significantly lower.

2. Load on low back during various tasks

In the questionnaire, the participants were asked whether SSL was effective for performing various tasks. Figure 9 shows the results. More than half of the participants in the comfortable group responded that SSL was effective for all the tasks. On the other hand, more than half of the participants in the uncomfortable group indicated that SSL was ineffective.

From these results, we can see that the subjective evaluation of the assistance provided by SSL depends on wear comfort. Causes of poor wear comfort include heat, tight fit and friction. By improving wear comfort, SSL can potentially receive better evaluations of its effectiveness in providing assistance.

TABLE IV MEAN VARIATION IN VAS

	Wearing SSL	Without SSL	Difference
Total (n=20)	30.1	29.5	+0.6
Uncomfortable (n=13)	34.4	28.4	+6.0
Comfortable (n=7)	22.1	31.5	-9.4

VII. SECOND TRIAL EXPERIMENT

A. Improvement

In response to the first trial experiment, we improved SSL as follows (Figure 10).
1. The neck hole was widened to avoid rubbing against the neck.
2. The vest was made larger to resolve a feeling of pressure.
3. A part of the vest was changed to a stretchable material to fit the wearer's body.
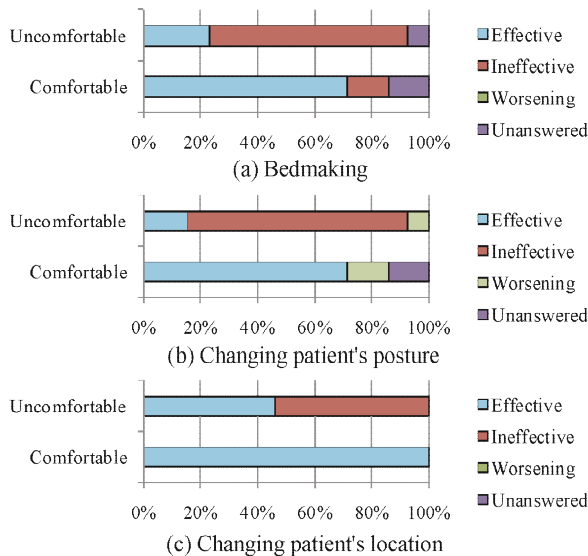
(a) Bedmaking

(b) Changing patient's posture

(c) Changing patient's location

Figure 9: Subjective load reduction
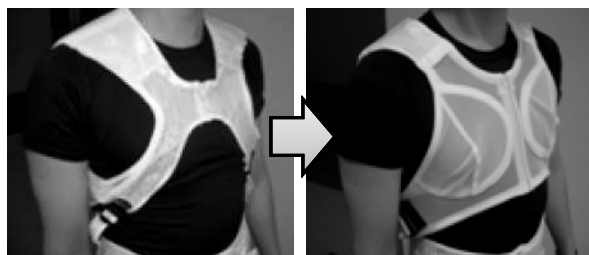for various tasks

Figure 10: Improvement of Smart Suit Lite

B. Experimental Conditions

To evaluate the effects of these improvements, we performed another trial experiment. Tables V and VI show the details of the experiment. Participants wore the old SSL and the improved SSL respectively, and evaluated fatigue due to work. In addition, because the assistive forces and mass of the improved SSL were almost the same as those of the old SSL, only the effects of wear comfort should reflect in the difference in the effectiveness of assistance.

C. Results

1. Wear comfort

Figure 11 (a) shows results for evaluation of wear comfort at three levels ("good", "normal" and "poor"). The number participants who indicated that wear comfort was "poor" decreased 25 percentage points in comparison with the old SSL. Therefore, a notable improvement in the wear comfort of SSL was achieved.

2. Lumbar load

Participants evaluated the effectiveness of SSL in reducing the load on the low back on a six-point scale (0,

"not at all effective"; 5, "very effective"). Figure 12 (b) shows the results. The mean score increased from 2.7 for the old SSL to 3.2 for the improved SSL. Therefore, SSL was notably improved in terms of the subjective reduction in load on the low back. In addition, participants evaluated fatigue on VAS as in the first trial experiment. The increase in average VAS value for work performed while wearing the old SSL was 16.4, whereas in the case of the improved SSL, this increase was 5.9; thus, for the improved SSL, suppression of the fatigue increase was 64.0% that for the old SSL.

The above results show that a significant improvement in the subjective effectiveness was achieved by improving the wear comfort of SSL. Therefore, the structure, materials and size variation of SSL should be further considered in the future.

TABLE V. EXPERIMENTAL CONDITIONS

Period	December 13–24, 2010
Type of facility	Internal medicine and rehabilitation
	(same hospital as first trial)
Number of participants	20 (caregiving staff members)

TABLE VI. OVERVIEW OF PARTICIPANTS

Sex	Female	19
	Male	1
Age	20s	1
	30–39	4
	40–49	2
	50–59	12
	60–69	1
Lumbar pain	Yes	7
	No	13

VIII. CONCLUSION

In this paper, we introduced a design method of Smart Suit Lite using a motion-based assist method, and designed and evaluated Smart Suit Lite for care workers.

Aiming to achieve an assist ratio of 25%, we developed a skin segment model for analyzing the change in length of the surface of the human body, and designed the arrangement and properties of the elastic belts of SSL for care workers. In addition, we have manufactured Smart Suit Lite in accordance with the above mentioned designs for elasticity properties and arrangements, and we have verified its assistive effects through basic experiments. The results of the experiments show an average reduction of 24% in the amount of activation of the erector spinae muscle, proving the effectiveness of the power assistance device. Moreover,
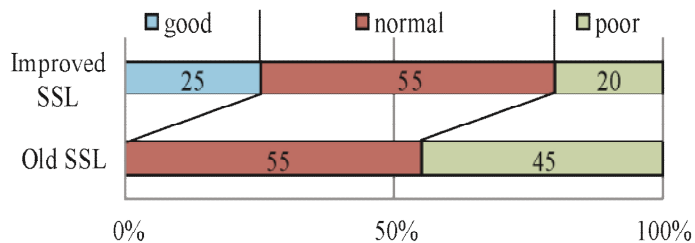
20 care workers at a hospital wore SSL while performing their duties, and evaluated its effectiveness in providing assistance. Poor wear comfort was found to lead to low subjective effectiveness of assistance. Therefore, we modified the SSL with the aim of improving wear comfort. As a result, 90% of participants reported a reduction in load on the low back. The subjective feeling of fatigue was found to depend on various factors including comfort and habituation, and thus further long-term evaluations will be necessary in order for SSL to be used routinely.

(a) Wear comfort

(b) Alleviation of load on low back

Figure 12: Evaluation

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Extraction of Neural Activation from Biological Spatio-temporal Imaging Data using Autoregressive Model-based Filtering Technique

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Abstract—**Regression and cross-correlation analyses have been widely used to detect neural activation in the dynamic brain imaging data. These analyses require a preliminarily assumed reference function, which reflects temporal changes in neural activation. In other words, only the neural activations, whose temporal patterns resemble to the reference function, can be detected. In cases which reference functions are hardly defined, these analyses are not applicable. In our previous study, we have proposed a method of spatio-temporal filtering to overcome these disadvantages. This method enables us to detect the time and region when and where dynamical state transition according to neural activation arises in repeatedly recorded data (multiple trial data). Moreover, we showed the capability to detect neural activation in single-trial data, such as recording of spontaneous brain activity, using sliding time window.**

Keywords-Spatio-temporal filtering; Innovation approach; Brain functional imaing; Optical imaging

I. INTRODUCTION

There have been developed many techniques for biological signal recording e.g., functional magnetic resonance imaging (fMRI) and optical recording, and they enable us to perform detailed investigation of neural activation. However, with the dimensions and size of the data becoming larger and the structure of the data becoming more complicated, a more efficient and automatic method for analysis is required.
One of the widely used methods is based on regression or correlation analysis to detect spatial information of neural activation pattern [1].

For the investigation of microscopic neural activation, an optical imaging technique has been used. This technique offers us the information of temporal transition of membrane potential in excitable tissue [2]-[4]. The structure of optical imaging data is three dimensional: two of them are for space and one is for time. Although the structure of optical imaging data is similar to that of fMRI data, there has been no widely used method for data analysis. Respect to this situation, Oku *et al.* [2], [3] and Okada *et al.* [4] applied time-lagged correlation analysis to optical imaging data to elucidate the mechanism of respiratory rhythm and pattern generation in the rat and frog brainstem. In the studies of rat brainstem [2], [4], they used 4th cervical

spinal cord ventral root (C4VR) output signals that are equivalent to phrenic inspiratory burst activity as the reference function, and found appearances of earlier and simultaneous activities relative to the output signals in the regions of respiratory rhythm generators.

The advantage of regression analysis or cross-correlation analysis is that the significance of the coefficients can be statistically evaluated. Moreover, the test values can be mapped on an anatomical image and it gives spatial information. However, still there have been several problems in these analyses. The regression or correlation analysis evaluates only the morphological resemblance between the time series and the reference function. If there is some activation pattern that does not resemble the reference function, then it cannot be detected. More seriously, in the case that the reference function cannot be defined, the data can hardly be analyzed by these methods.

In the field of time series analysis, innovation approach has been efficiently applied to detect the changes in signal dynamics. The dynamical properties of stationary time series, whose statistical properties, e.g., mean value and variance, do not depend on time, can be identified using mathematical models such as autoregressive (AR) model and autoregressive moving average (ARMA) model [12]. Let us suppose that we prepare two time series; one is used as test time series for model identification, and the other is for filtering with the identified model. If new time series is filtered through the identified model, unpredictable signals remain in residuals. The residuals are called innovations. If the amplitude of innovations of filter output becomes significantly higher than the innovation of test data, the state is detected as a phase transition of dynamics in the system. This approach has been applied in various fields, e.g., plant monitoring system [5]-[9].

In this session, we will review our previous works which applied the innovation approach to optical imaging data attempted to detect biological activation in innovations and introduce methods to evaluate statistical significance of the activation for multiple-trials and single-trial data [10][11].

The methods to detect biological activation is explained in Section II. Section III provides the information about the imaging data which was analysed in this paper. Section IV presents the detected activation using AR model based

filtering method and compare the performance with time-lagged cross-correlation analysis.

II. METHOD

A. Time-lagged cross correlation analysis

The time-lagged cross-correlation analysis provides temporal information of the appearance of the signals in the imaging data whose wave forms resemble pre-defined reference function [2]. Suppose $\eta^v(t)$ is a time series of imaging data for a pixel $v = (l, m)$ and $\varphi(t)$ is a pre-defined reference function, the time-lagged cross-correlation can be denoted as

$$R^v(\tau) = \eta^v(t)\varphi(t-\tau) / \sqrt{\overline{(\eta^v)^2}}\sqrt{\overline{\varphi^2}}, \qquad (1)$$

where τ is a relative time lag. The lagged correlation coefficient can be straightforwardly converted to a t-value. Then time dependent correlation t-map can be obtained if this procedure is repeated for all pixels. In the case $\tau = 0$, it will be ordinary cross-correlation analysis.

B. Autoregressive(AR) model

There exist many models used for the analysis of time series. The most commonly used model for time series data is the autoregressive (AR) model. The autoregressive process is a difference equation determined by random variables. The most simplest AR model is the first order autoregressive model, written as AR(1), which considers the immediate past value $\eta(t-1)$ to determine the present value $\eta(t)$. An example of AR(1) model is denoted as

$$\eta(t) = 0.8\eta(t-1) + \varepsilon(t), \qquad (2)$$

where $\varepsilon(t)$ is a white noise series with zero mean and variance σ_ε^2.

An example of second order AR model is denoted as

$$\eta(t) = 1.8596\eta(t-1) - \eta(t-2) + \varepsilon(t). \qquad (3)$$

The autoregressive (AR) model for a time series $\eta(t), t = 1,...,S$, can be generalized to the p-th order AR model, which is defined as a linear combination of the past values with a prediction error $\varepsilon(t)$ and a constant β,

$$\eta(t) - \beta = \sum_{i=1}^{p} \alpha(i)\eta(t-i) + \varepsilon(t), \qquad (4)$$

where $\alpha(i)$ are AR coefficients. The linear dynamic properties of the system can be identified with a parameter vector $\boldsymbol{\vartheta} = \{\alpha(1),...,\alpha(p),\beta,\sigma_\varepsilon^2\}$, here σ_ε^2 is a variance of $\varepsilon(t)$.

In the case of AR(2) model, the relation between AR coefficients and oscillation frequency f can be denoted as

$$\alpha(1) = 2r\cos\left(2\pi\frac{f}{Fs}\right), \ \alpha(2) = -r^2, \qquad (5)$$

where, Fs is a sampling frequency and r is a length of radius in the Gaussian plane which corresponds to attenuation coefficient. For example an oscillation with $f = 3[\text{Hz}]$, $Fs = 50[\text{Hz}]$ and $r = 1$ can be realized with (3).

The AR coefficients in (4) can be estimated from actual data by least square method, Yule-Walker method and so on[12]. And the optimal model order p can be decided by Akaike Information Criterion (AIC)[12][13].

C. Filtering using AR model

Suppose the AR model is written as,

$$\varepsilon(t) = \eta(t) - \sum_{i=1}^{p} \alpha(i)\eta(t-i), \qquad (6)$$

it can be interpreted as a filter whose input is data and output is prediction error. The prediction error is also called innovation. In the case the frequency for filtering is previously known, the AR coefficients can be adjusted by (5). If the AR coefficients are estimated from actual data, the innovation time series contains the signals which cannot be predict from the vibration characteristic of the data.

The most widely used filtering method is the Fourier-based filtering method to eliminate specific frequency components. Here, the difference between the Fourier-based filtering and AR model based filtering with simulated data. The simulated data was generated by (3) and impulse I was applied as unpredictable signal with AR (2) process,

$$\eta(t) = 1.8596\eta(t-1) - \eta(t-2) + \varepsilon(t) + I. \qquad (7)$$

The impulse $I = 1$ was applied at 3.0[ses] ($t = 150$) and continuously during the period of 4.0-5.0[sec] ($200 \le t \le 250$). Fig. 1 (a) and (b) show the simulated time series and output signal from Fourier-based band stop filter (2.5 – 3.5 Hz). Though there can be observed a cusp point at 3[ses] ($t = 150$) in the output signal which correspond to the timing of applied impulse, it is hardly recognized without prior information about the timing. And the onset and offset of continuously applied impulse during 4-5[sec] ($200 \le t \le 250$) are not clearly detected. A new AR (2) model was applied to the period of simulated data 0

– 1.0 [sec] and the model was identified with estimating coefficients. And the rest part of the simulated data was filtered through the identified AR (2) model. Fig. 1(c) shows the output signal from the AR (2) model, i.e., innovation times series. Unlike the result from Fourier-based filtering, the amplitude of the innovation time series was steeply increased at the time and the period impulse was applied. This method is called innovation approach.

For the analysis of biological signals, the biological activation can be detected using the AR model based filtering method. However there is possibility that some noise or artifact is also detected. In order to discriminate biological activation and noise or artifact, the amplitude of innovation time series has to be statistically evaluated with repeatedly recorded data. Fig. 2 shows the transition of the amplitude of innovations for all repetitions. The area A is a set of the innovations within the period for model identification and the line B is a set of innovations of filter output at the time t' . We evaluated the statistical significance of the difference of mean amplitude of the innovations in area A and on line B using standard t-test.

signals were window-discriminated to yield Transistor-Transistor Logic (TTL) pulses and used to trigger the optical recording system. Total number of recorded time frames were 1024/256, the recording was started at 768/64 frames before the trigger signal, and repeated 30/34 times for data1/data2, respectively. Among these repetitions, 29 and 27 repetitions, which were contaminated with relatively small artifacts, were selected for data1 and data2, respectively.

Fig. 3 shows the recorded area in the brainstem, which contains two putative rhythm generators those which have been reported as the para-facial respiratory group (pFRG) [12] and the pre-Bötzinger complex (preBötC) [16]. Inspiratory-related respiratory activity was monitored from the C4VR with a suction electrode. The raw nerve signal was amplified, band-pass filtered from 15 Hz to 3 kHz, full-wave rectified, and integrated with a decay time constant of 100ms. This integrated signal was used as the reference function for the cross-correlation analysis. Further experimental condition and preprocessing were explained in [10].

Figure 2. Temporal transition of the amplitude of innovations for all simulated data (30 repetitions). The area A is the set of the innovations within the period of model identification and the line B is the set of the innovations of filter output at the time t' .
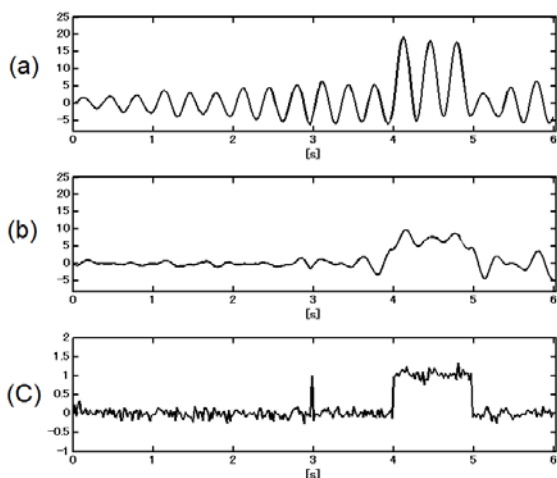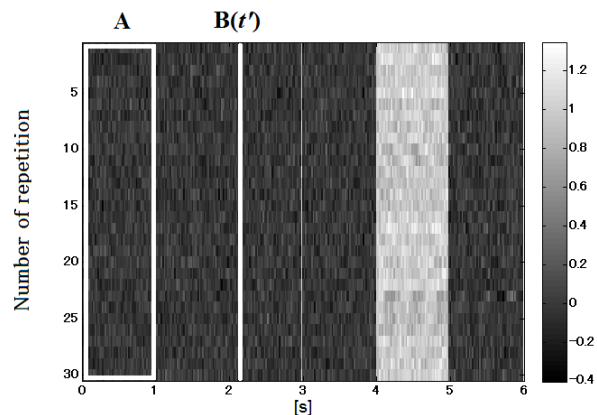

Figure 1. (a) Simulated data with AR(2) process (impulse was applied at 3.0 sec. and continuously during 4.5 – 5.0 sec). (b) Output signal from Fourier-based band stop filter (2.5 Hz – 3.5 Hz) (c) Innovation time series from AR(2) model

III. BENCHMARK DATA

We selected the same imaging data set from 2 day and 0 day old rats (corresponding to data1 and data2 respectively in this study) that was used in the study of developmental aspects of the respiratory neuronal activation in the rat brainstem [2] in order to evaluate our method by comparing its outputs with those of the time-lagged cross-correlation analysis.

Optical signals were sampled at 50 Hz (20 ms/frame) for data1 and data2. Analog signals of raw and integrated C4VR activities were recorded at 1 kHz for data1 and data2. These analog signals were amplified and digitized, then stored in a hard disk together with optical signals. Analog

IV. RESULTS

In the case when imaging data are repeatedly recorded, we obtain multiple time series $\eta^w(t)$, $t = 1, \ldots, S$, for each pixel ($w = (l, m, n)$, l and m are the indices of a pixel, n is the index of the repetition, $1 \leq n \leq N$) (Fig. 4). The signal from a pixel is contaminated irregular reflection light and scattered light from neighbouring pixels. In order to reduce these contamination, we consider following exogenous type AR model.

Suppose the measurement points of the imaging data are on the two dimensional pixel that are labeled by an index $v = (l, m)$ and only the influences of nearest neighbor upon each pixel are considered as exogenous inputs, the ARX model will be specialized as

$$\eta^v(t) - \beta^v$$
$$= \sum_{i=1}^{p} \alpha^v(i)\eta^v(t-i) + \sum_{u \in N(v)} \sum_{j=1}^{q} \delta^u(j)\eta^u(t-j) + \varepsilon^v(t), \tag{8}$$

where $N(v)$ is a set of indices of the neighbor pixels to the pixel at $v = (l,m)$. Suppose neighbor pixels are restricted to the pixels, which contact with the edge of the pixel at the point v, a set of indices of neighbor pixels will be

$$N(v) = \{(l+1,m),(l,m-1),(l,m+1),(l-1,m)\}. \tag{9}$$

The ARX model with the restricted neighbor pixels will be referred as Nearest Neighbor Autoregressive model (NNAR) in this paper. The innovations for the pixel at v,

$$\varepsilon(t)^v = \eta^v(t) - \hat{\eta}^v(t) \tag{10}$$
$$= \eta^v(t)$$
$$- \left(\sum_{i=1}^{p} \alpha^v(i)\eta^v(t-i) + \sum_{u \in N(v)} \sum_{j=1}^{q} \delta^u(j)\eta^u(t-j) + \beta^v \right)$$

contain the signals which cannot be predicted by a linear AR process even though the spatial influences from the neighbors are taken into consideration.

Suppose the NNAR model is identified with a limited period $t_1 \le t \le t_2$, any arbitrary selected other period $t'_1 \le t \le t'_2$ can be filtered through the identified NNAR model. Let the innovations corresponding to the period for the NNAR model identification and for filtering $\varepsilon^{1,w}(t)$ and $\varepsilon^{2,w}(t)$, respectively. The amplitude level of $\varepsilon^{2,w}(t')$ will increases at the time point t' when the unpredictable signals arise. Then the statistical significance can be evaluated by comparing the mean value between the innovations at t', $N^{-1}\sum_{n=1}^{N} \varepsilon^{2,(l,m,n)}(t')$ and whole innovations within the period $t_1 \le t \le t_2$, $(N(t_2-t_1))^{-1}\sum_{t=t_1}^{t_2}\sum_{n=1}^{N} \varepsilon^{1,(l,m,n)}(t)$ by some statistical test. In this study, we employed standard t-test for this purpose. By shifting time point t', time-dependent t-values can be computed. Then time-dependent activation t-map, which shows dynamic state transition, can be obtained by repeating this procedure for all pixels.

This method detects not only biological activation as dynamic state transition but also some artifact inevitably. Some procedure for artifact discrimination has to be considered. There are mainly two types of artifacts. One is stationary oscillatory noise such as those caused by electric power supply (hum noise) and mechanical vibration of measurement system. This sort of artifacts can be identified by AR-type model, and then $\varepsilon^{1,w}(t)$ will be close to Gaussian white noise. Therefore the oscillatory noise will not appear in $\varepsilon^{2,w}(t')$, because these artifacts consist of predictable signals. The other is caused by non-stationary sporadic noise, and it will appear in $\varepsilon^{2,w}(t')$ because it cannot be predicted by the identified AR-type model. This sort of artifact can be partly removed from final results such as activation t-map by setting a threshold for spatial cluster size and/or duration.
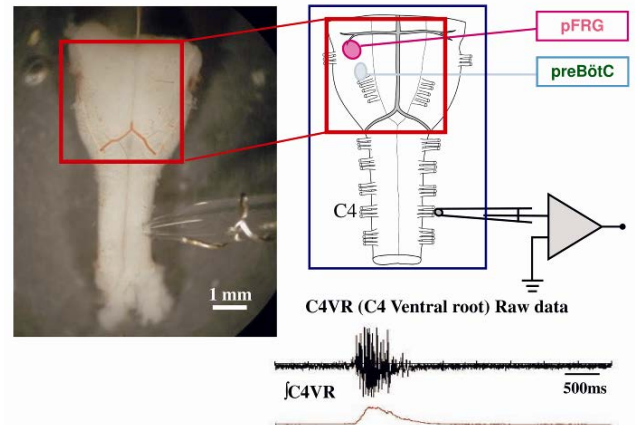

Figure 3. (a) Ventral brainstem area for optical imaging (surrounded by the red square), (b) Schematic representation of anatomical structure of the brainstem and the recorded area, (c) Raw output signal from C4VR, (d) Integrated C4VR output signal.

Background stationary oscillations were identified by a NNAR model on the period sufficiently before or after the respiration onset. In this study four neighboring pixels, which contact with edge of a pixel of interest were employed for the NNAR model for saving the computational cost. The parameters in the NNAR model were estimated using the least square method. Then the rest part of the data was filtered through the identified model and the innovations were estimated. We defined the origin of time axis as the onset of respiratory activity observed in the C4VR signal. The NNAR model was identified on the period sufficiently before the onset of respiratory activity, i.e., from -4.22s to -2.24s (100 time frames). Subsequently, the period from -2.22s to 5.24s (374 time frames) was filtered for the data 1.

In principle, model order of the NNAR model should be optimized according to some criterion, such as Akaike Information Criterion (AIC) [13] for each pixel. However, since it would not be appropriate to individually optimize the model order for a large number of pixels, a common value should be chosen. It is important to choose a sufficiently large value, lest any relevant correlations in the data should be missed. On the other hand, too large model orders may cause over-fitting problems and reduce the reliability of the estimated model parameter values. In this study, the model order for p and q in (10) was fixed to the

same values for the simplification of the model. Then, we gradually increased the model order from two and found that stationary oscillations were properly identified and removed from the innovation by NNAR model with $p = q = 7$. Therefore, we conclude that for our data a model order of this value represents a good compromise.
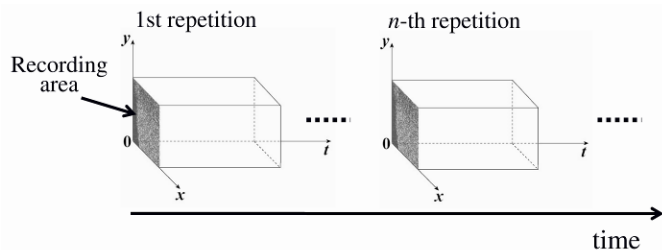

Figure 4. Conceptual representation of the structure of the optical imaging data. The recorded imaging data can be reconstructed with three dimensional data (two dimensional space corresponding to recording area and time axis) for each repetition.

We evaluated the statistical significance of the difference of mean amplitude of the innovations in the period of model identification and filter output by the method mentioned with Fig. 2. This procedure was repeated for all pixels, and then temporal transition of activation t-map was illustrated. Five representative time frames of activation time map are illustrated as time dependent t-maps in Fig. 8(c), which shows the area and time at which significant dynamic state transition arises. The activation initiated at the caudal part of pFRG, corresponding to the rostral ventrolateral medulla (RVLM) [14] and [15], and then extended rostrally toward the rostral part of pFRG and caudally toward the preBötC. Subsequently the activation traveled to more caudal structures of the brain. Finally the activation of the high cervical spinal cord reached its maximum (Fig. 5(c) in the time frame at 0.24s) just before the peak of C4VR output signals (Fig. 5(d)). Further, a line from preBötC toward caudal brain structures could be seen in Fig. 5(c) in the time frame at 0.64s. This sequence may correspond to the fact that caudal brain structures such as ventral respiratory group (VRG) contain premotor and motor neurons that relay respiratory outputs to the C3-5 segments of the spinal cord with a certain time delay.

Fig. 5(a) displays activation t-maps for the raw imaging data instead of the innovations using the procedure described above. Although both images for the imaging data and innovations were thresholded at the same level, significant areas for the imaging data were less than those for the innovations. Further, the propagation from the preBötC toward caudal brain structures could not be detected in activation t-maps for the raw imaging data.

The results of correlation analysis with averaged imaging data across repetitions is illustrated in Fig. 5(b) as correlation t-maps. The respiratory related activated areas, such as pFRG and preBötC, were effectively detected. However, the duration of detected activations was shorter

than that of activation t-maps for the innovations. Besides, the propagation from the preBötC toward caudal brain structures could not be detected.

Data2 did not have enough time frames before the onset of respiratory activation because of the parameter setting for setting recording condition. Therefore the analysis cannot be applied to data2 under the same condition for data1. In order to solve this problem, the NNAR model was identified at the period sufficiently after the onset of respiration, i.e., from 1.98 to 3.96s (100 time frames), and then the period from -1.12 to 1.96s (155 time frames) was filtered. The activation t-maps for the imaging data and innovations are illustrated in Fig. 6 (a) and (c), respectively. The correlation map is shown in Fig. 6 (b). The analyses yielded similar results to those for data1. Furthermore, the time lag of the activation between preBötC and VRG could be clearly detected in the activation time map for the innovations (Fig. 6 (c) in the time frames of 0s and 0.26s), which was not distinct in the correlation map (Fig. 6 (b)).
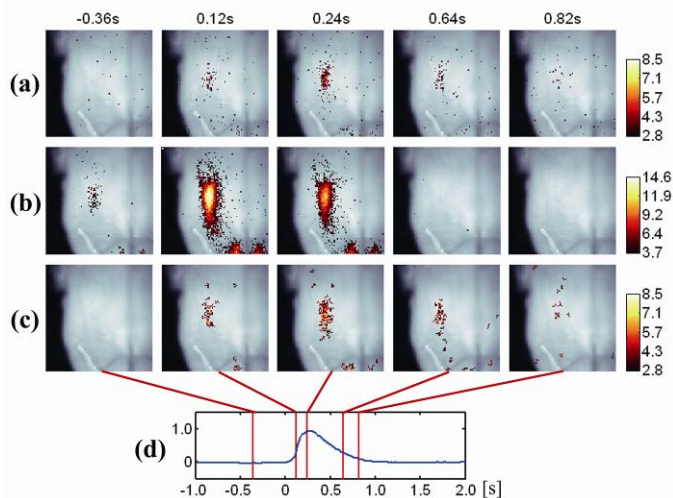

Figure 5. Representative time frames of temporal transition of the activation t–maps for the imaging data (a) and the innovations (c), and the correlation t–map with averaged imaging data across repetition (b). The C4VR output signal and time points corresponding to the time frames (d). The t-maps were thresholded of $p<0.05$ (corrected by the False Discovery Rate (FDR)) and a cluster extent of five pixels.

Fig. 2 shows the temporal transition of the amplitude of innovations that was estimated in the simulated data. In the case of the data with single repetition, the line B will consist of only one innovation. Therefore, mean amplitudes of the innovations in the area A and on the line B cannot be statistically evaluated because of the insufficient number of samples. Nevertheless, our method is applicable if the line B is replaced with a time window in order to obtain sufficient number of samples, i.e., innovations, although there is a trade-off with respect to temporal resolution. In this study, we employed a sliding time window $t' - (w/2) \le t' \le t' + (w/2)$ (w: even integer) and the difference of mean values of the innovations within the sliding window $(t_2 - t_1 + 1)^{-1} \sum_{t=t_1}^{t_2} \varepsilon^{1,\nu}(t)$ and the period for

NNAR model identification

$$\left(t_2 - t_1 + 1\right)^{-1} \sum_{t=t_1}^{t_2} \varepsilon^{1,\nu}(t) \quad (t_1 \le t \le t_2)$$ was evaluated using *t*-test. Then, we could obtain time dependent *t*-value with sifting time t'. We empirically selected the width of sliding window at $w = 30$. Fig. 7 (b) shows activation *t*-maps for five representative time frames from a repetition in data1. The regions of pFRG and preBötC were successively detected and its spatio-temporal distribution pattern is similar to the Fig. 5 (c). Fig. 7 (a) displays activation *t*-maps for the raw imaging data instead of the innovations. The square of the detected regions was smaller than the *t*-maps from innovation time series.
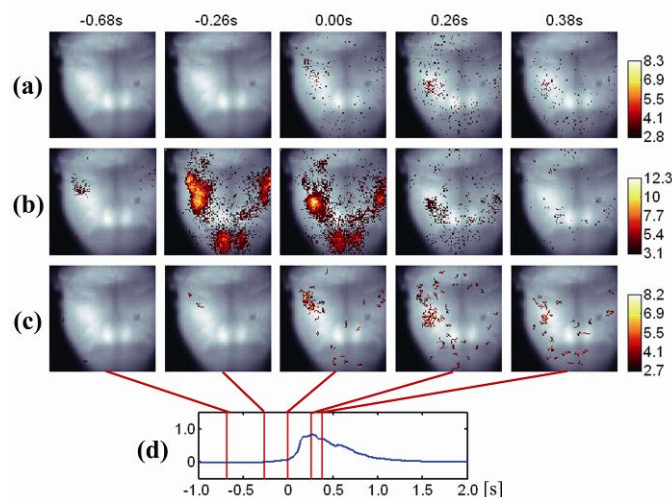
Fig. 8 illustrates temporal fluctuation of the *t*-values the point A – D in Fig. 7 (a) and (b) where neural activations were clearly observed in the *t*-maps. At the point A, the fluctuations of the *t*-values from both raw data and innovations have similar pattern, and exceed the threshold level about 0.28sec later than the onset of inspiration. At the point B and D, only *t*-values from the innovation exceed threshold level. The neurons around this region start to activate about 0.1sec earlier and 0.8 sec later than the onset of inspiration respectively. At the point C, the difference of *t*-values from the raw data and the innovation is remarkable. There can be seen clear neural activation about 0.1 sec after the onset of inspiration.

V. DISCUSSION

Using the ordinary cross-correlation analysis, which is equivalent to the time-lagged cross-correlation analysis with a restriction $\tau = 0$, only one of the two respiratory rhythm generators, the preBötC, was detected with data2. The result can be seen in Fig. 9(b) in the time frame at 0.00s. The reason why the other respiratory rhythm generator was missed is that the activation of pFRG appeared earlier than the onset of the C4VR activity in the reference function. Therefore significant correlation was not found between pFRG and C4VR signals. In this situation, time-lagged cross-correlation analysis gave a solution. Oku, *et al.* [2] applied this method to the optical imaging data and reported an earlier respiratory activation in the pFRG (Fig. 6(b)).

However, there are still several problems in the ordinary or time-lagged cross-correlation analysis. First, it does not consider dynamical properties of time series, but evaluates only morphological resemblance between the two time series. Therefore, only pixels whose temporal activity pattern has a similar shape to the reference function can be detected.

Figure 6. Representative time frames of temporal transition of the activation *t*–maps for the imaging data (a) and the innovations (c), and the correlation *t*–map with averaged imaging data across repetition (b). The C4VR output signal and time points corresponding to the time frames (d). The *t*-maps were thresholded of *p*<0.05 (corrected by the False Discovery Rate (FDR)) and a cluster extent of five pixels.
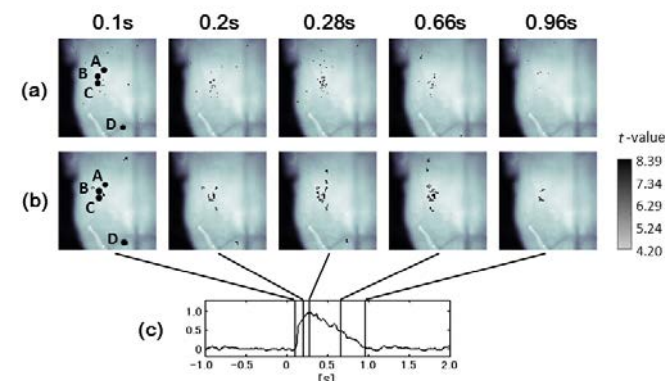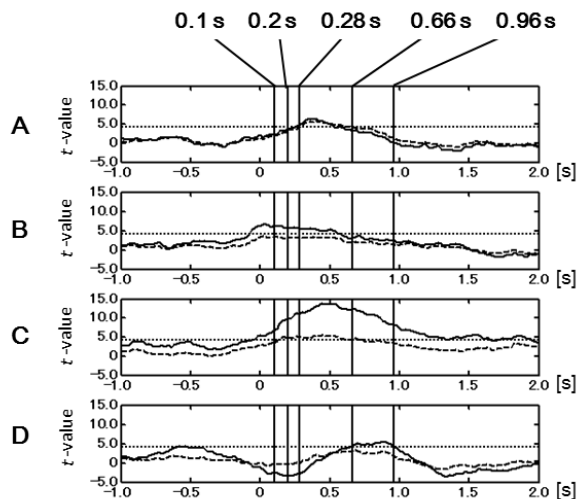

Figure 7. Representative time frames of temporal transition of the activation *t*–maps for the imaging data (a) and the innovations (b) The C4VR output signal and time points corresponding to the time frames (c). The *t*-maps were thresholded of *p*<0.05 (corrected by the False Discovery Rate (FDR)) and a cluster extent of five pixels.

Figure 8. Fluctuation of the *t*-values from the raw data (broken line) and the innovations (solid line). The horizontal dotted line indicates threshold level $t = 4.1950$ (*p*<0.05) (corrected by the False Discovery Rate (FDR))

Second, it has been applied only to averaged imaging data across the repetition of means. Any method has not been proposed that can be applied to each repetition nor statistically evaluated across the repetition of the measurement. Third, in the case of the time-lagged correlation analysis, the larger the time lag is, the shorter the overlapping length of the two time series becomes. Then, inaccuracy of the analysis will increase with larger time lags. Fourth, the absolute time point of the appearance of activations cannot be investigated by time-lagged cross-correlation analysis. This is because the origin of time axis is defined arbitrarily. Therefore the correlation *t*-map of averaged imaging data and activation *t*-map for innovations cannot be compared on the common time axis. If the time point corresponding to the peak of C4VR signal is selected as the origin of time frame for the time-lagged cross-correlation, the time point of the onset of activations in the correlation *t*-map and activation *t*-map will agree.

Our method is free from the above-mentioned problems. Namely, our method can sensitively detect the spatio-temporal emergence of activations through the investigation of the dynamic state transition and statistical evaluation across the repetition of the measurement. The earliest activation is localized in RVLM (the caudal part of pFRG), which can be seen typically with data2 (Fig. 6(c) in the time frame at -0.26 s). The activation extends bidirectionally to the rostral part of pFRG and to the preBötC region and travels to the high cervical spinal cord (Fig. 5(c) in the time frame at 0.64s, and Fig. 6(c) in the time frame at 0.26s).

We conclude that our method can precisely detect the biological activation without employing additional information such as reference time series data, and the significance can be evaluated with statistical test values. Further, it can be generally used to spatio-temporal data, e.g., functional magnetic resonance imaging (fMRI), electroencephalography (EEG), near infrared spectroscopy (NIRS).

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