# Chapter 10
# Case Studies

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**Abstract** Information and Communication Technologies—as analyzed in this book—could allow a radical change in the way healthcare services are delivered to the citizens and could represent an effective tool to cope with the today's healthcare challenges.

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In this chapter we introduce two European research projects where large part of the concepts addressed in this book are applied; they are the MICHELANGELO project of the seventh Framework Program and CHIRON of the ARTEMIS JU Program.

The CHIRON project (Cyclic and person-centric health management: Integrated approach for home, mobile and clinical environments) focuses on prevention i.e. on a move away from 'health care' towards 'health management', from 'how to treat patients' to 'how to keep people healthy', from a "reactive care" to a "proactive care". CHIRON designed a system's architecture making possible a "continuum of care" i.e. an integrated health management approach in which health is patient-centric at home, in the hospital and in nomadic environments. Care is moved from the hospital to the home and the healthcare staff is enlarged by adding informal carers to the medical professionals and by motivating and empowering the patient himself to manage his own health. Moreover the CHIRON system builds a personalized risk assessment of the patient by integrating personal information, data gathered at home and in a mobile environment through an innovative set of wearable sensors and data available at the hospital including outcomes of image-based tests. The expected results are a reduction of the healthcare costs and a better quality of care.

MICHELANGELO addresses a specific category of patients i.e. the autistic children; the aim is to use ICT to promote and facilitate the assessment of autism within the home setting, away from the traditional clinical environments and to provide personalized "home-based" intervention strategies. This is achieved through the provision of cost-effective, patient-centric home-based intervention remotely controlled by the therapist (remote rehabilitation). The proposed method aims at enhancing the effectiveness of the treatment through its "intensiveness" and "personalization" matching the individual characteristics of autistic children and the involvement of the parents in their "natural" home environment in the role of "co-therapists".

Both projects offer interesting inputs on how Information and Communication Technology could help in "revolutionizing" healthcare. It is worthwhile to highlight that both projects keep the doctors at the core of the healthcare process and in both of them technology is not replacing the experience and the competences of the medical professionals and is not removing the needed physical contact between them and the patients but it supports the doctors in executing their tasks in a more effective and better way.

This chapter is split into two parts: in the first we will introduce the two projects mainly from a strategic perspective in line with the current efforts towards "radical changes" needed to cope with the heavy challenges the healthcare system is facing.

The second part gives a technological insight of the CHIRON project and shows how this project is deploying several of the concepts analyzed in the previous chapters of this book.

This part presents the architecture of an integrated continuous monitoring system for Cardiovascular Disease (CVD) patients in nomadic settings developed under the ARTEMIS-JU CHIRON Project. The proposed sensor platform constitutes of commercially available subsystems effectively integrated into a single multi-sensor non-invasive wearable solution. To enable medical experts to assess the patient's condition remotely, a number of analysis algorithm were developed and implemented into an Android application in order to provide the desired medical information. The key challenge in the development of these algorithmic solutions, was to balance the expected performance while maintaining a low level of power consumption, thus facilitating the continuous monitoring purpose of the system. Furthermore, a web-server based framework provides medical experts with an interactive analysis and monitoring interface and provides the infrastructure for storing the obtained data.

## 10.1   Part 1: Two European Research Projects for the Healthcare of the Coming Years—The CHIRON and the MICHELANGELO Projects

**Silvio Bonfiglio**

### 10.1.1   Introduction

As an effective response to the current challenges in healthcare we need a radical change of the way healthcare services are delivered to the citizens; we need to move the care of the citizens from the hospital to home to take benefit from the availability of informal caregivers and enable a more affordable healthcare service by reducing the need of hospitalization. This will translate into early intervention when the economic impact of the disease is still low.

The previous chapters of this book have shown how advanced ICT-based solutions applied to medicine (what we call e-health) could contribute to the achievement of the ultimate goal i.e. a better quality of care at more affordable costs.

In this chapter we analyze two European research projects representing interesting case studies, the CHIRON project of the ARTEMIS JU Program, and the MICHELANGELO project of the FP7-ICT. Both projects emphasize the active role of patients and citizens, promote a person-centred healthcare with the patient at the core of the overall process and recognize the individual, specific characteristics of each patient.

CHIRON addresses the entire healthcare chain and proposes a new approach and a reference architecture fostering a continuum of care; the MICHELANGELO project focuses on the treatment of children suffering from Autism Spectrum Disorders and introduces ICT and cost-effective, patient-centric home-based intervention remotely controlled by the doctors to promote the assessment and the therapy of autism within the home setting, away from the traditional clinical environment.

The overall chapter is divided in two parts. In the first part the strategic views of the CHIRON and MICHELANGELO projects are described to give the reader a flavor of the possible broad spectrum of applications and how a remote healthcare

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system could be applied in practice within that spectrum. The second part is more technology orientated. Here we restrict ourselves within the detailed description of the CHIRON system only because of the fact that it represents an excellent example of an advanced remote healthcare system developed by the joint effort of Industry, Academia and Research Institutes. In this case we start from the basic functional requirements of the system and show in step-by-step fashion how the complete end-to-end system is developed. Without loss of generality, such an approach could be followed for developing any applications orientated remote healthcare system.

## 10.1.2  The CHIRON Project

Healthcare is facing demographic and socio-economic challenges: from an ever ageing population suffering from chronic diseases and various handicaps to the need for affordable "global" healthcare provided by fewer and fewer professionals and medical infrastructures for critical, often mobile, patients.

Moreover medicine is confronted by the "age of globalization": the movement of people all over the world along with societal and economic developments means that medical professionals have to deal with new diseases, new symptoms and new contextual factors relevant to the health of the citizens, such as changed environments, new nutritional habits and lifestyles.

Healthcare—traditionally focused on institutional care and on curing diseases (diagnosis, treatment, rehabilitation)—needs to shift towards monitoring, risk assessment and early detection to effectively manage chronic diseases and to reduce complications at least. We need a shift from "health care" (how to treat patients) to "health management" (how to keep people healthy).

CHIRON (Cyclic and person-centric health management: Integrated approach for home, mobile and clinical environments) is a European research project of the ARTEMIS JU Program and is addressing these issues; it has received funding from the ARTEMIS Joint Undertaking under grant agreement #100228 and from the National Governments participating to the project.

Twenty-seven Organizations from eight European member states and representing the industry (large companies and SMEs), the research and the academic communities and medical institutions are involved.[1] Having started in March 2010, the project has a term of 45 months and a budget of 18 million Euro.

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[1] The following Organizations are participating at the CHIRON project: FIMI Srl, Universities of Bologna, Genova, Roma, Trieste, CNR, I + Srl, ITS, SELEX ES, W-LAB Srl from Italy; ALMA, ATOS, CEIT, CIMNE, Ibermatica,Tecnalia from Spain; Athena ISI and Intracom from Greece; BARCO from Belgium; Philips Healthcare and ZorgGermak from The Netherlands; University of Budapest from Hungary; Jozef Stefan Institute and Mobili from Slovenia; Cardionetics, Southampton University Hospitals NHS Trust and University of Southampton from United Kingdom.

**Fig. 10.1** CHIRON
addresses the complete
healthcare cycle



The project addresses one of the today's societal challenges i.e. "effective and affordable healthcare and wellbeing". CHIRON combines state-of-the art technologies and innovative solutions into an integrated framework of embedded systems for effective and person-centred health management throughout the complete healthcare cycle, from primary prevention (person still healthy) to secondary prevention (initial symptoms or discomfort) and tertiary prevention (disease diagnosis, treatment and rehabilitation) in various domains: at home, in nomadic environments and in clinical settings (Fig. 10.1).

It applies several of the approaches and techniques discussed in the previous sections of this book.

In currently applied healthcare practice, a disease is commonly discovered after symptoms have emerged. Only then, people become patients and apply for medical care, a diagnosis is made and a treatment is proposed and initiated. CHIRON fosters a change in this approach i.e. a shift towards an earlier diagnosis based on the risk assessment of the still healthy person (Fig. 10.2).

In CHIRON, detection and diagnosis are based on the analysis of heterogeneous medical data that originate from personal data of the patient, medical past knowledge, imaging systems, collection of vital sign data through sensors and handheld devices. Medical doctors having remote access to the person's health record are able to take a more proactive role in prevention of diseases.

This is a significant innovation compared to the currently used approaches that are based on health-related parameters only, often monitored *instantaneously* and *episodically* (during clinical center visits). In addition CHIRON intends to explore the correlation across physiological, psycho-emotional and environmental parameters.

The CHIRON system involves modeling at different structural and functional scales, combining inputs from sensor data, medical imaging, clinical diagnoses,
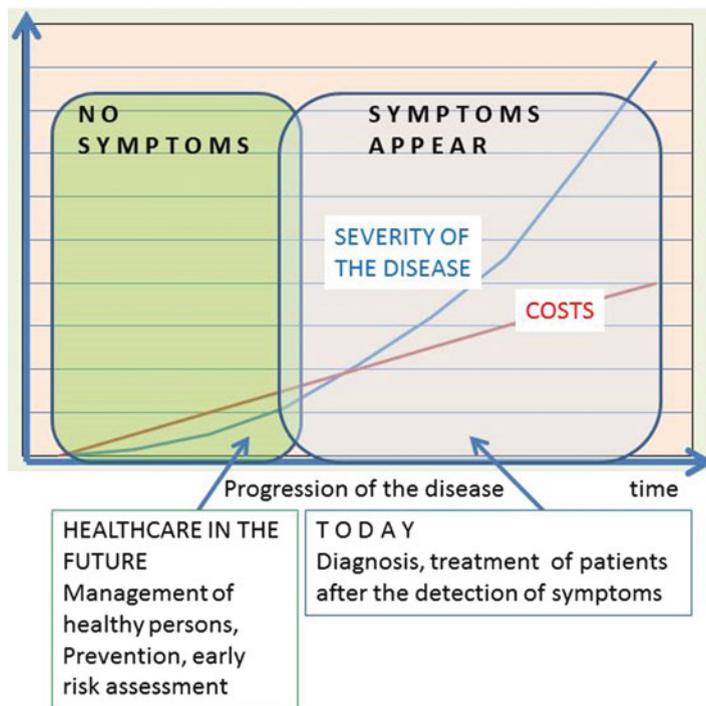
**Fig. 10.2** From treatment of patients to early risk assessment and management of still healthy persons

patient history and population-level statistical information. Continuous and close-to-the patient remote monitoring of physiological and psycho-emotional state and trends are integrated and contextualized with environmental parameters, information on patient activity and lifestyle related factors. The CHIRON reference architecture ensures interoperability between heterogeneous devices and services, a reliable and secure patient data management and a seamless integration with the clinical workflow.

A new way of looking at impending risk is constructed, based on simple measures obtained on a continuous basis with time-frame acquisitions, processing and relation with future events depending on the type of variable considered: heart rate, skin and ambient temperature and humidity, daily weight, water and urine variations and in house movements (Puddu et al. 2012).

It is worthwhile to notice that such a correlation model does not exist in practice; presently diagnosis of a disease depends largely on the experience of the individual doctors. The typical models for diseases only predict mortality or morbidity in long term but never identify "when actually" the person is at risk.
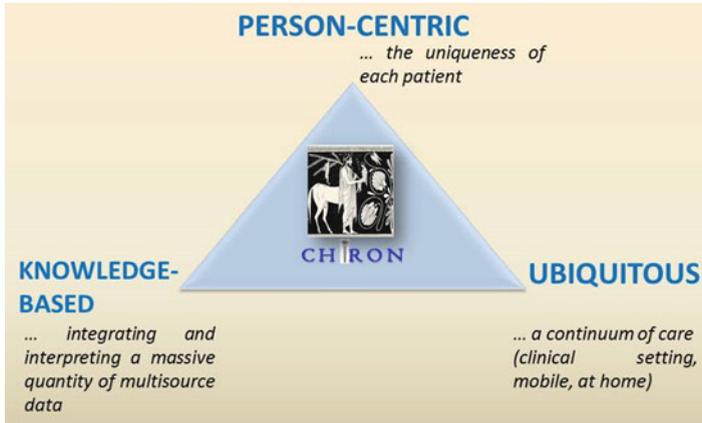
**Fig. 10.3** The basic concepts of the CHIRON approach

### 10.1.2.1 The CHIRON Concepts

In the field of e-health CHIRON represents an interesting case study since it applies innovative approaches made possible by advanced ICT solutions of which some already addressed in this book. More specifically the CHIRON research work is based on three main concepts (Bonfiglio 2010; ARTEMIS Joint Undertaking 2010):

(a) The realization of a "continuum of care" i.e., addressing in an integrated approach health management at home, in the hospital and in a nomadic environment.
(b) A "person-centred approach" where the needs of the citizens, the medical professionals and the whole community are at the core of the design and the uniqueness of each user is fully recognized ("personalized healthcare") including the use of proactive solutions anticipating the needs of people, adapting themselves to context and taking the required actions and thus enriching quality of life and fostering independence.
(c) A knowledge-based system integrating past and current data of each patient together with statistical data related to the whole community in a large and distributed repository (in CHIRON called *Virtual Data Repository*) and promoting a move towards prevention and early risk assessment (Fig. 10.3).

A. Care at home and everywhere ("continuum of care")
A continuous multi-parametric monitoring of physiological and psycho-emotional state, environmental parameters, patient activity and lifestyle related factors has been realized and the best compromise between unobtrusiveness and accuracy of the gathered data was pursued in designing it.
Measurements provided by the close-to-the patient remote monitoring are incorporated into physiological models and fused with anatomical and

functional information derived from MRI and 3D ultrasound data, from which organ-level models are built and updated.

All these data—integrated with those available in the Hospital Information System—contribute to the building of an evolving Patient Health Profile and to the definition of a personalized and constantly updated risk assessment model (identified in CHIRON as *Alter Ego*).

In the CHIRON architecture, high emphasis is given to the seamless integration of the personal health platform with the clinical workflow and the integration of the personal and medical data gathered in a "non-clinical setting" into the electronic health record of the patient. Adherences to standards with regard to the exchange of the medical information (HL7 v.3) as well as reliable and secure patient data management are key issues. Semantic interoperability is realized.

### B. A person-centric healthcare management

CHIRON provides personalization in the delivery of the healthcare services. The "one size fits all" paradigm will no longer apply, especially when it comes to medicine. Personalization will also feature in a coaching system to help the patient to reduce immediate risk and improve long term recovery. Patients are empowered and motivated to self-manage their wellbeing. This person-centred approach puts the needs of the citizens, the medical professionals and the whole community at the core of the CHIRON design. Health is considered a value the single person and the whole community have to build and preserve.

The user profile represents an evolving model of the relevant aspects related to the health of a user and provides a continuously up-to-date risk assessment of his health status.

### C. A knowledge-based medicine—Support to the doctors

To make a diagnosis, to define the most suited treatment for the patient, the physician needs to make use of a massive quantity of data, aggregated from different large data sets, interpreted and integrated with community related statistical data and past knowledge. Moreover he needs to take timely decisions.

All these data represent the outputs of multiple and heterogeneous devices and subsystems ubiquitously distributed: physiological signs and activity information are gathered through unobtrusive on-body sensors and are contextualized with environmental parameters measured by discrete devices; results of lab analyses including image-based examinations are available in the information systems and PACS systems of the clinical centres and hospitals, epidemiological/statistical datasets and past knowledge are dispersed everywhere all across the world and sometime organized and stored in various repositories. In CHIRON all of them—integrated in the *Virtual Data Repository* (*VDR*)—provide medical professionals with an effective support for early diagnosis and personalized treatment planning.

A critical aspect CHIRON addresses, is the effectiveness and the intuitiveness of the feedback provided to the medical professionals, avoiding the risk of overloading the doctors with a plethora of data. CHIRON interprets and
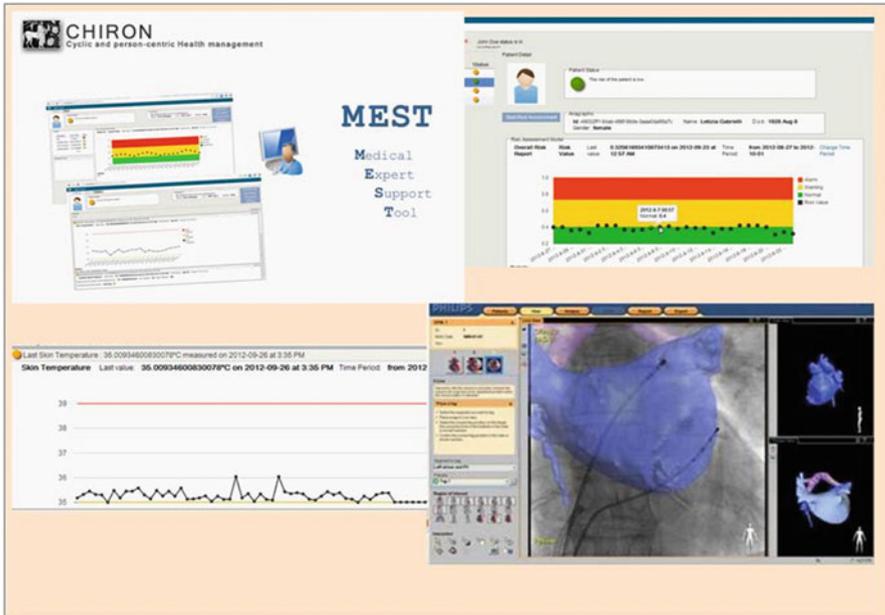
**Fig. 10.4** Intuitive and effective feedback to the doctor

translated those data into features. An ontological approach is used to retrieve information from multiple distributed content repositories and present it in a structured and aggregated manner giving the doctor an easy and powerful tool for immediate understanding of the status of the patient (Fig. 10.4).

We are aware that technology cannot replace the experience of the medical doctors but can support them in taking the most appropriate and timely decision. In CHIRON the doctor remains the protagonist of the healthcare process and the only owner of the clinical decision.

### 10.1.2.2 The CHIRON Architecture

In the CHIRON architecture all the devices/subsystems generating, interpreting and storing data are embedded modules of an overall complex system; each of them has the computing and memory capabilities to execute a specific task for which the outputs of other sub-systems are needed. The task of each of these embedded blocks could be very simple such as processing the raw data, removing artefacts and extracting features. Tasks may also be complex such as that of a medical image acquisition system or an image-guided surgical system.

In contrast to the typical architectures and keeping in mind the energy constraint of a sensor node, specialized low-complexity algorithms for on-board signal

denoising, artifact removal, intelligent classifier and feature extraction were realized for each of the electrophysiology sensors. It was done without compromising the medically trustworthiness quality of the captured signals.

In this network of embedded systems Internet provides the communication infrastructure for the exchange of information among them and the weaknesses of Internet in terms of quality, reliability and real time interchange of the information are compensated by a higher autonomy and robustness of each of the modules of the system. Each block is capable of operating independably even in the presence of network degradation or temporary failure and is able of executing a minimal, essential task autonomously (e.g. the prompt warning of the patient if a vital sign is above the allowed threshold or the activation of an emergency call in the case of a critical event).

In this regard, the CHIRON project realizes the vision driving the European ARTEMIS JU Program i.e. a world in which smart "objects" have "a presence in cyber space, exploit the digital information and services around them, communicate with each other, with the environment and with people, and manage their resources autonomously" (ARTEMIS Joint Undertaking 2011). CHIRON intends to contribute to the realization of this vision in a so important and complex domain such as the healthcare one. Being the citizen and his quality of life at the core of the healthcare model proposed by the project, the CHIRON system—even if specifically designed for healthcare—interoperates across many application domains. CHIRON uses a middleware which allows to achieve not only interoperability between heterogeneous devices and services and exchange of multisource information across the whole healthcare cycle but also a multi-domain compatibility.

### 10.1.2.3 Technological Challenge and Innovation in CHIRON

The project promises to progress beyond state-of-the art in several disciplines (Bonfiglio 2011) such as healthcare architecture, sensor nodes with enhanced capabilities, new methods and algorithms for the measurement of physiological parameters, advanced solutions for the analysis and the visualization of medical images.

The technological challenges of the full integration of a Personal Health System into the conventional hospital-based Healthcare System are related to the realization of the best synergy among conflicting requirements such as:

- Data gathering and data processing in resource-constrained systems (the wireless mobile sensors network),
- Non-invasiveness of the monitoring combined with accuracy of the measured data,
- Continuous monitoring vs. the acceptance of the solution by the patients,
- Automation or minimal human intervention vs. the reliability of the feedback,

- Availability of a massive quantity of data vs. the easy and fast interpretation of these data by the medical professional,
- Privacy and security of data vs. easy and ubiquitous access to these data by authorized persons, etc.

The advanced solutions proposed by CHIRON represent a solid contribution to solve these issues. More specifically CHIRON developed:

(a) Sensor nodes with enhanced capabilities (multi-parametric monitoring, local processing, energy harvesting and power management),
(b) Innovative methods for the measurement of biological parameters (ECG, blood pressure with enhanced accuracy, serum potassium concentration in the blood),
(c) Advanced solutions for the analysis and the visualization of medical images,
(d) A dynamic and personalized risk assessment model (*Alter Ego*),
(e) A distributed data storage approach (Patient's Virtual Data Repository) with enhanced data security and privacy provisions.

In the current age of image-centred medicine the new advanced tools developed in the CHIRON project are expected to facilitate real time processing, computer-aided detection and accurate visualization of medical image as well as to support doctors in making accurate diagnosis by reducing the risk of a "false negative" or the need for additional and costly examinations due to a "false positive".

### 10.1.2.4   Conclusions

The CHIRON research project contributes in promoting a new way of delivering healthcare services and promotes a paradigm shift from diagnosis and treatment of patients based on symptoms to diagnosis of patients based on risk assessment of healthy persons.

Moreover CHIRON intends to contribute to the uptake of a market still in its nascent phase, the e-health one, identified by the European Commission as a "*lead market*" where "innovative products/services/solutions have high growth potential, where EU industry can develop competitive advantage and where action by the public authorities to deal with regulatory obstacles is needed".

CHIRON contributes to bridge the gap between R&D and market readiness.

The healthcare societal challenges will promote the creation of new and innovative services/products and the solutions and the technological advances made in CHIRON will contribute to the uptake of applications such as medical imaging, personal healthcare (home and mobile monitoring), health management and coaching, wellbeing, clinical decision support systems and healthcare informatics.

The move towards "global, open networks of multi-domain embedded systems" will lead to radical changes in the business processes, by asking for cross-company collaborations.

### 10.1.3   The MICHELANGELO Project

#### 10.1.3.1   Background

The MICHELANGELO project is co-financed by the European Commission (Framework Program 7—Grant Agreement # 288241). It aims to use emerging technologies to design personalized home-based intervention strategies for children with Autism Spectrum Disorders. MICHELANGELO brings together an interdisciplinary team of eight partner organizations in Italy, Malta, United Kingdom and France and bridges academia, industry, research and clinical practice.[2]

In the diagnostic manual used to classify disabilities (the DSM-IV of the American Psychiatric Association), 'Autistic Disorder' (AD) is listed as a category under the heading of 'Pervasive Developmental Disorders (PDD)'. It affects thought, perception, attention and social interaction and—rather than one disorder with a well-defined set of symptoms—it represents a broad spectrum of disorders that ranges from mild to severe (Autistic Spectrum Disorders—ASD).

According to a recent study (Pediatrics 2009) the prevalence of Autism Spectrum Disorders (ASD) in the young population has increased in USA from the 0.6–0.7 % of the previous 2003 estimate in excess of 1 % (i.e. from 1 in every 150 children to 1 in every 91 children). A similar situation has been reported in Europe where the prevalence of autism in children increased from the 0.5–0.7 % (Atladottier et al. 2007) to 1.16 % as reported by Kuehn (2007) and by several other studies. These trends have considerable social and economic impacts. The average lifetime costs for a person with autism were evaluated at approximately 5.7€ million for people with low functioning autism and 1.5€ million for people with high functioning autism (Knapp et al. 2007).

Consolidated data on the prevalence of autism in Europe is lacking. Variability in reported data is often due to methodological factors; the result is that 'there is no comprehensive or comparable data at EU level concerning the incidence or prevalence of this disease' (report of the European Commission dated 2004). In reviewing various prevalence studies, Williams JG at al. found that 50 % of the variation among study estimates could be explained by factors such as age of the screened children, diagnostic criteria used, country, rural or urban location, etc.

Equally in Europe the social and economic burden of ASD has not been adequately recorded, as epidemiological figures are unreliable and inconsistent. In a recent report, the economic consequences of autism in the UK were calculated and the findings reveal that children with autism cost £2.7 billion (3.8€ billion) annually, yet for adults the figure is £25 billion (36.2€ billion)—over eight times as much.

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[2] The following Organizations are participating to the MICHELANGELO Projects : FIMI S.r.l., Italian National Research Council (CNR), Fondazione Stella Maris and I+ Srl (Italy); University of Southampton and University of Ulster (United Kingdom); University Pierre et Marie Curie, and Assistance Publique-Hopitaux de Paris (France); Across Limits Ltd. (Malta).

It is well accepted in the scientific community the importance of an early diagnosis of autism and that prognosis is greatly improved if a child is placed into an early intensive and highly structured educational program by age of 3 years old. Early treatment is a crucial step to ameliorate some of the symptoms associated with autism and some investigators have reported that this is a critical developmental period in a child's life during which brain's plasticity is maximal and environmental influences can interfere with neural connections (Dawson 2008; Oberman et al. 2008; Altemeier et al. 2009; Dawson et al. 2010). Moreover, researchers agree on the inadequacy of one single treatment approach for all the children with ASD due to the heterogeneity and the developmental nature of the disorder. Earlier identification of children with ASD and the development of personalized and evolving protocols for intervention could increase the effectiveness of the treatment. Both these objectives could be achieved with the support of the technology as developed in the MICHELANGELO project. Moreover researchers are starting to develop **prosthetic technologies** able to help children with autism by supplementing or replacing the natural capacities. Advances in key technology areas such as affective computing and wearable computing offer a lot of potential for computer-based prosthetic tools.

### 10.1.3.2 The Michelangelo Project: Concepts and Objectives

Typically, the assessment of the status of the child with autism and the delivery of a number of therapeutic interventions are executed within a clinical setting. Often this approach implies a reduced effectiveness mainly in consideration of:

(a) The "artificial" context of the lab-based environment, which generates the potential for artifacts and adds systematic and non-systematic bias to the findings, therefore potentially producing results that do not reflect behaviors in real life.
(b) The lack of "intensiveness" of the therapeutic intervention (just a few hours per week) limiting its beneficial effects, as demonstrated in some recent studies (Remington et al. 2007).
(c) The poor "individualization" or "personalization" of the intervention protocol, due to a lack of the *a priori* knowledge of which treatment method will be most effective for a specific child.

The MICHELANGELO Project aims to address and overcome these aforementioned considerations by moving, as much as possible, the assessment and the therapeutic interventions from a clinical setting to a more "natural" home environment and by using non-obtrusive or minimally invasive techniques. As an example, quantitative EEG (QEEG) analysis has proved its capability of identifying dysfunction in various regions of the brain in children with autism. Electroencephalogram (EEG) measures brain waves; it shows the variations in electrical potentials at a number of scalp sites. Inside the brain neurons produce their own electrical fields; it is thought that an unhealthy brain will have large changes in the electrical potential

compared to the potentials produced by a healthy brain. A brain map (quantitative QEEG) could give useful information.

Unfortunately the invasiveness of the currently used systems induces both systematic and non-systematic biases to the experimental outcome eluding the actual nature of the brainwave behaviour and connectivity.

MICHELANGELO intends to minimise the biases and modulation effects by making the recording system pervasive in nature so that the patients becomes "unaware" of its presence; it will allow the patients to move freely in their "own" environment while at the same time offering them naturally occurring stimuli and continuously monitoring their EEG activities.

In the pervasive wearable EEG system (a cap of just 60 g weight) being used within MICHELANGELO, the risk for poor accuracy due to the limited number of the employed electrodes (19 electrodes), and to the portability of the system is reduced as much as possible by calibrating and adjusting the system according to the specific clinical child to be monitored. Throughout the Project, wearable EEG recordings has been correlated with those of a dense-array EEG system used as "golden standard" and the wearable model adapted and "customized" through the optimization of the processing algorithms. In this way, a suitable characterization of the brain connectivity of the child and a timely detection of abnormal brain waves activity become possible.

Similar studies (Laibow et al. 2001) have reported a change of parameters such as heart rate, systolic and diastolic pressure, pulse rate, sweat index, body temperature, fingertip temperature, electro-dermal activity (EDA) as an effect of the progress in the rehabilitation program of patients with brain injury. In the MICHELANGELO 'system' a set of wearable and non-invasive sensors will facilitate the monitoring of ECG parameters also.

Equally important to the quality and accuracy of the interventions and therapies is the fact that the MICHELANGELO approach will be extremely cost effective as a result of the limited involvement of the medical professionals in spite of the intensiveness of the treatment.

Another important objective of the MICHELANGELO Project is to open new opportunities in the field of 'personalized' autism research and treatment. Although most researchers agree on the fact that it is necessary to establish an individualized treatment for each child, very little is known about how to individualize treatment protocols, there have been very few studies in which different methods have been validated and compared and there is a little knowledge on how to determine *a priori* which intervention is more likely to benefit individual children.

ICT can provide a rich understanding of the requirements of each individual and allows to monitor them as they develop. It is about realizing a system that recognizes that every child is unique and exhibits unique symptoms and needs and that interventions and therapies need to be tailored according to that.

The MICHELANGELO Project aims to increase the knowledge in these fields by comparing the effect of different methods.
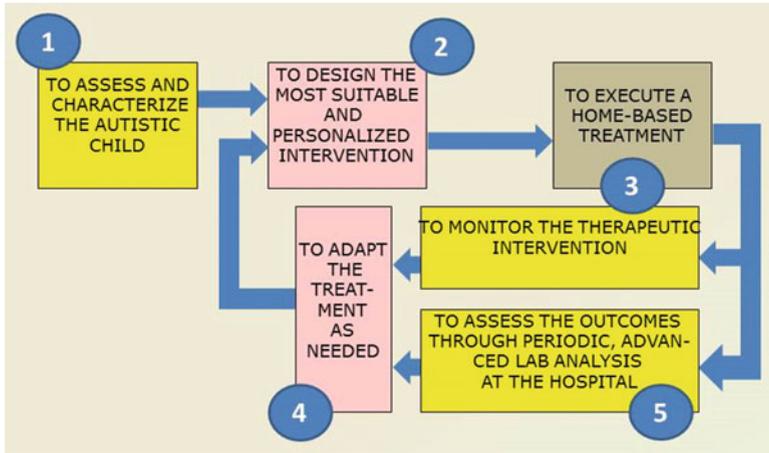
**Fig. 10.5** The MICHELANGELO approach

### 10.1.3.3 The Five Steps of the Michelangelo Approach

In the diagnosis, characterization and treatment of the children with autism the Project proposes an approach that will include the following core steps (Fig. 10.5):

1. The characterization of the child with autism
In the specialised medical center a multimodal and unobtrusive system including video observation, audio signal analysis, QEEG and other physiological signals monitoring (such as heart rate) synchronized all together is used in a controlled environment (the "*Michelangelo room*") to observe reactive behaviours of children with autism. The developed system allows the analysis and annotation (automatic, semi-automatic or manual annotations) of recorded video captured during the observations. Advanced solutions allow to maximize the automation of the system in detecting "events" i.e. behaviours of the observed child indicating a response to the proposed stimuli. The annotations referring to specific behaviours of a child are correlated to changes in the characteristics of the captured signals. In such a way personalized indicators of the brainwave functionalities under different naturally occurring stimuli are identified. Real time feedbacks are given to the therapist to allow him to adapt—when needed—the therapeutic approach and the interaction with the child during the session.
Furthermore multi-modal coordination and interactional synchrony will be analyzed to get useful insights into the level of rapport between social partners. We employ both audio and video analysis to monitor the rhythm and the convergence of actions (including communicative and motor functions). The system enables to evaluate statistically significant correlations between actions (from both intra- and inter-personal points of view) and produces an interpretable representation of the coordination during interactions (Delaherche and Chetouani 2010).

The stimuli able to generate a response in the child's brain are analyzed further on
through the combined use of the wearable Q-EEG system and of an eye-tracking
system. Each one of them is presented to the child on the screen of a PC,
equipped with an eye tracker which tracks the movement of the child's eyes
and records their fixations. At the same time, the brain wave activities are
recorded via Q-EEG. Different image processing schemes can be initiated on
the acquired scenes and this will make it possible to determine the nature of the
stimulus resulting in the brain wave behaviour.

2. Developing an appropriate patient-centric intervention protocol

Once the above mentioned activities are completed, the findings can be used for
developing appropriate patient-centric intervention protocol. MICHELANGELO
intends to explore the benefits of a heterogeneous intervention strategy combining
neuro-feedback and developmental/behavioural interventions.

Joint attention and imitation tasks are incorporated in a set of serious games with a
level of difficulty that evolves depending on the progress of the intervention and
on the response of the child. The project is developing a methodology for easy
adaptation and personalization of the games.

3. Therapeutic intervention in a natural environment and the unobtrusive
observation of the child

The child is monitored during his/her normal daily activities, moving freely within
a controlled environment while wearing the "QEEG cap" and the other physio-
logical sensors. The QEEG system detects abnormal brain waves and trigger a
microcamera integrated into the QEEG cap with the objective of tracking the
specific objects, situations generating this specific brain activity or a change in
the monitored physiological parameters. Data monitored at home are transmitted
periodically to the remote Medical Center for further analysis.

Serious games are proposed to the child and the quality of the execution of the
planned tasks is automatically assessed by the system and made available to
the doctor.

4. Adaptation of the therapeutic intervention

On the basis of the gathered information, the doctor assesses the intermediate
outcomes of the therapeutic intervention and adapts it by giving information
and training about the change to the parents of the child. In addition to the
periodic sessions at the medical center, remote meetings are planned between
the therapist and the parents to share observations, opinions and to strengthen the
cooperation between them.

5. Periodic assessment at hospital

In MICHELANGELO the "at-home monitoring" is combined with periodic advanced
lab examinations. The project plans to develop new methods for a better analysis of
the anatomical and functional brain's connectivity based on magnetic resonance
images (DTI and fMRI techniques). They allow a better assessment of the evolu-
tion of the disorder and of the effect of the therapy.

### 10.1.3.4   Expected Advance Beyond the State-of-the Art

The MICHELANGELO Project intends to go beyond the state-of-the art in the assessment of ASD and the intervention protocols by making possible a remote and effective "at-home management" of the autistic children. The recent introduction of new equipment such as QEEG-, eye-tracking-, diffusion tensor imaging-based systems and of wearable biomedical devices is providing differential frames to seize invaluable insights, to test hypotheses and collect data that shed new light into the nature of typical and atypical developmental processes of social cognition.

MICHELANGELO project will contribute by introducing advanced solutions such as:

- A pervasive wearable EEG system in conjunction with an eye-tracking system to record brain wave behaviour when the patient is presented with a number of naturally occurring stimuli. According to our knowledge it is the first time that these technologies are used together and that eye tracking is used to better define the therapeutic intervention rather than to assess and/or diagnose the disorder;
- A wearable, unobtrusive multi-sensorial platform for the continuous monitoring of vital signs able to detect behavioural changes in the autistic children;
- An audio- and video-based system monitoring interactive patterns of the child at both motor and communicative levels to detect multi-modal coordination and interactional synchrony and get useful insights into the level of rapport between social partners;
- A multimodal solution for the patient's treatment where neuro-feedback and developmental/behavioural intervention techniques are used at home and designed in such way to combine an intensive intervention and the avoidance of heavy involvement of the clinicians and therefore to be cost effective;
- A set of specifically developed serious games and techniques for the assessment of the quality of execution of the game and for the adaptation of its level of difficulty and its personalization;
- A personalization of the overall therapeutic intervention and its timely adaptation—in a closed loop approach—according to the feedbacks from the autistic child and the intermediate outcomes of the intervention.

Moreover MICHELANGELO intends to explore and to assess emerging ICT-based therapeutic techniques such as 3D and virtual reality, computer vision, and robotics-based methods.

Progress beyond the state of the art is expected also in specific technological areas such as:

(a) An advanced system for the analysis and the annotation of recorded videos and synchronized QEEG, physiological and audio signals.
(b) Sophisticated signal processing algorithms to remove the redundancies present in the traditional Principal Component Analysis (PCA) used to characterize the brain connectivity.

(c) A decision support system helping the therapist in assessing the status of the disorder and the response of the child to the presented stimuli and in adapting and personalizing the therapeutic intervention accordingly.
(d) Advanced techniques and image processing solutions for the analysis of anatomical and functional brain connectivity made respectively with Diffusion Tensor Imaging (DTI) and Functional Magnetic Resonance Imaging (fMRI). The use of these techniques for the assessment of Autism Spectrum Disorders and specifically applied to autistic children represents a new field of research.

### 10.1.3.5  Medical, Social and Economic Impact

A. Medical Impact
The MICHELANGELO project aims at improving the management of ASD in children by transferring the treatment from the clinical setting to the more comfortable environment of their own homes. There, an intensive and monitored treatment and more "natural" conditions will ensure a more accurate assessment of the evolution of the disease and will allow a timely adaptation and personalization of the therapeutic treatment. The clinical exploratory study planned in the last year of the project will provide a rich set of information that will enhance the medical knowledge related to ADS and to the role ICT could play in autism. It will include the use of state-of-the art ICT solutions (3D, virtual reality, robotics) for enhanced developmental/behavioral interventions combined with neurofeedback-based protocols. Moreover, the outcomes of the project will contribute to a research in the ASD field that is still in its infancy i.e. the "a priori" definition of the right treatment for each individual patient ("individualization of the treatment") and will allow to collect a large quantity of data related to ASD.

B. Social Impact
The project intends to contribute to the management of ASD, a disease with serious socio-economic impacts and heavy consequences affecting not only the patient but all the family members. The MICHELANGELO solution will enable children with autism to stay in the comfort of their homes, thus reducing costs related to therapeutic interventions in external infrastructures with clear benefits for the families and the overall community. The final objective will be to enhance the chances for a gradual rehabilitation of the autistic child and his inclusion in the community. The user-centric approach of the MICHELANGELO Project will foster a user-friendly design and minimise the intrusiveness of technology. By transferring the therapeutic intervention from the hospital to home—it emphasizes the role of the parents and of the educators and fosters the cooperation between them and the medical professionals; they will participate all together to the care process of the autistic child.

C. Economic Impact

The MICHELANGELO approach combines intensiveness of the treatment (no longer limited to few hours a week at the therapist's office or at the hospital) with cost effectiveness due to the automation of the treatment asking for a minimal intervention by the doctors, even if they are enabled to seamlessly supervise, follow-up and monitor the autistic children during the evolution of their therapeutic program at home. The MICHELANGELO project helps to put in place early therapeutic interventions and it will result in cost saving. As it was observed in the EAIS (European Autism Information System) final report (European Autism Information System (EAIS) (2006–2008)) "the latter is the intervention in the affected child's life, the greater the time and costs involved in providing healthcare and support services".

### 10.1.3.6 Conclusions

The MICHELANGELO project addresses main societal needs related to health as highlighted by the European Commission such as "affordable healthcare through cost reduction, new technologies for patient monitoring, diagnostics and treatment that allow for better, faster and more cost effective care". It opens new horizons and exploits ICT and other technologies in assessing and treating pervasive developmental disorders with specific focus on autistic children.

## 10.2   Part 2: The CHIRON Project—A Technological Insight

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### 10.2.1   Introducing the Proactive Approach in CVD

World Health Organization (WHO) reports indicate that Cardiovascular diseases (CVD) is the most common cause of death in the world accounting for 30 % of all-cause deaths. Recent estimates predict that CVD dominance will continue to raise leading to over 20 million deaths in 2015 (Frost and Sullivan 2009). The already high associated cost for the treatment and long-term care of CVD patients is also expected to follow an incremental trend. As an example the cost for

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CVD-related treatment in the E.U. countries is 169€ billion per year, of which 62 % accounts for direct healthcare costs (Dickstein et al. 2008).

By taking into account the related productivity loss and informal care represent 21 and 17 % of the overall CVD costs respectively it is evident that CVD poses a formidable socio-economic burden for developed countries. Due to these facts, current conventional care delivery systems are under serious strain with the risk of reaching unsustainability in the future unless a pioneering shift in the care delivery approach of disease management is initiated. The concept of *Proactive Care* instead of the conventional *Reactive Care* approach has been highlighted as the most effective model for care delivery in years to come which will enable pre-emptive medical intervention and management by prognosticating an impending episode even before the full manifestation of the symptoms, leading to a significant decrease in death and hospitalization rates.

For the implementation of such a proactive care system, capturing, processing and information fusion of heterogeneous physiological data on a continuous manner in nomadic settings, is a key element. This will be followed by the constant interpretation of the acquired data in a "context-aware" way utilizing established medical knowledge. Recent achievements in Information and Communication Technology (ICT), in particular in the area of Wireless Sensor Networks (WSN), mobile communication and sensor technology have the potential of developing the necessary technological background of such a remote healthcare system that is capable of delivering cost-effective high-quality ubiquitous healthcare. The key challenge in the design of such a system is associated with the resource constrained nature of wireless embedded nodes, which are typically battery-powered devices with only basic processing capabilities. On the contrary, the requirements of a remote healthcare monitoring system involve significant computational tasks, since almost continuous radio communication and signal processing of data is essential. Hence, in order to achieve long-term, uninterrupted, operation of such a system the limited resources of the sensor platforms must be utilized effectively.

This chapter discusses the development and evaluation of such a remote healthcare solution focused on the uninterrupted monitoring of CVD patients. The entire system was developed under the Cyclic and person-centric Health management: Integrated appRoach for hOme mobile and clinical environments (CHIRON) Project. The proposed system constitutes of on-body Electrocardiogram (ECG), temperature, sweating index and activity sensors while an Android-based smart phone acts as the communication gateway and computational platform. In order to facilitate the desired long-term system operation, the designed algorithms for the analysis of the physiological data are characterised by their low-complexity which maximizes the system's lifetime. Dedicated firmware has been developed for implementing the sensors operation and their communication with the smartphone.

According to a review on remote monitoring solutions for CVD patients previous approaches present several limitations (Klersy et al. 2009). The majority of them makes extensive use of home devices, or ignores parameters that have been medically established as indicators of an impending critical cardiovascular episode, like skin sweating or ST-segment shift with heart rate changes. These documented shortcomings prompted the development of the CHIRON remote monitoring system.

In the rest of this chapter, the clinical requirements of the proposed system are initially presented in Sect. 10.2.2, with the overall system architecture analysed in Sect. 10.2.3. The design of the individual system components are described in Sect. 10.2.4 while the system integration and its interaction with the Information processing platform are discussed in Sect. 10.2.5. The Medical Analysis and Storage subsystem is analyzed in Sect. 10.2.6 and conclusions are drawn in Sect. 10.2.7.

## 10.2.2   *Clinical Requirements of a* **Proactive** *Remote CVD Monitoring System*

The fundamental purpose of a *Proactive* CVD monitoring system is to provide clinicians with the necessary physiological data and medical parameters for remotely assessing the patient's overall cardiovascular condition with an acceptable degree of confidence. Clearly since the work presented here focuses on CVD, capturing and analyzing the ECG is of paramount importance. Of the same importance as the ECG trace itself, is a number of clinical parameters directly derived from the ECG signal. These metrics, are extensively used in clinical cardiology and their value is extracted from the temporal position and amplitude value of the constituent waves of the ECG waveform. Other vital signs proven to be significant for cardiovascular monitoring and thus included in the CHIRON system, are the patient's skin temperature and skin sweating index. Moreover, in the CHIRON system it was decided that an activity recognition mechanism coupled with the calculation of the equivalent metabolic energy value, consumed during activities has to be included. Activity data can play a key role in assessing and managing the patient's health status. The inclusion of activity and metabolic energy expenditure information, is also expected to facilitate the correlation analysis among the monitored parameters which may ultimately provide novel predictive features that can act as early warnings and lead to medical intervention before the full manifestation of a critical episode (e.g. myocardial infarction). To the best of our knowledge the CHIRON sensor platform is the first attempt in developing a fully-integrated solution capable of remotely monitoring all physiological signals required for the evaluation of CVD (Pantelopoulos and Bourbakis 2010).

In order for the system to satisfy its purpose, the aforementioned physiological parameters should be monitored in a continuous manner over extended periods of time during the day. This is the pivotal point of the *Proactive Care* approach as it allows to capture the variation in the value of these parameters over time, which is considered by medical experts to be the key approach in the attempt to capture the decline of the patient's health and to a further level the prediction of an imminent critical episode.

These clinical requirements posed by the *Proactive Care* approach yield certain engineering and technological challenges that must be addressed. Firstly, extensive uninterrupted monitoring necessitates the development of a non-invasive, having a maximum of three straps attached to the body's patient, low-power solution able to

effectively and robustly communicate the vital signs and relevant parameters from the point of acquisition to the clinician's remote location. In essence, long-term refers to a system capable of acquiring and processing information for up to 6–8 h during the day. This timeframe is dictated from the fact that CVD patients will not tolerate to bear such a system for more time during the day. To accommodate the clinical requirements described in this section, a customized sensor-platform and its corresponding system architecture was developed and presented in details in the following sections.

### 10.2.3  System Architecture

The sensor platform of the CHIRON system comprises of four sensor devices. Specifically, one ECG single-lead sensor, one temperature/sweating index (TS) sensor and two 3-axis accelerometers are employed. From the data captured by the two accelerometers the patient's activity and energy expenditure are derived. The four sensor devices are embedded in three sensor modules, powered with rechargeable batteries, attached to two elastic straps, resulting in a total of three separate platforms positioned in the patient's body. The first strap is a chest belt designated to be attached in the patient's upper abdomen/lower thorax area containing the ECG module and an integrated accelerometer-temp/sweat (ATS) module. The second strap places the second accelerometer module on the patient's thigh area. The three sensor modules collect readings from the four sensors and transmit them wirelessly, using the wireless Bluetooth (BT) standard, to the information processing platform (IPP). A pictorial representation of the wearable sensor system is provided in Fig. 10.6.
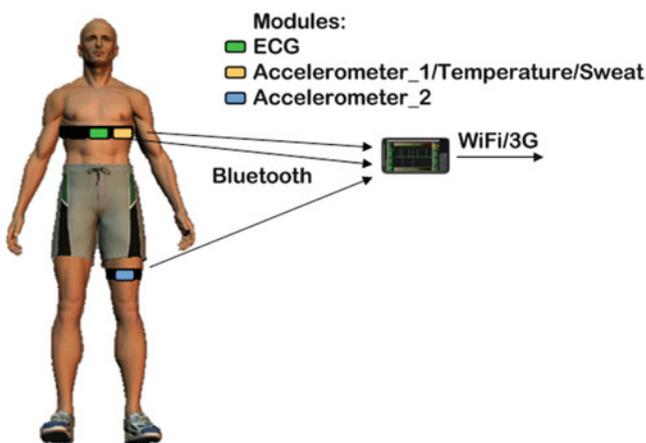


**Fig. 10.6**  The configuration of the integrated wearable sensor platform

The IPP constitutes an Android-based smartphone, tasked with fusing and processing the incoming sensor data while also providing the user interface. Apart from the TS data the rest of the sensor readings are subjected to specific signal processing for the extraction of the clinical ECG parameters, the identification of the patient's activity and finally the calculation of the energy expenditure. For these operations a customized Java-Android application (pIPP) was developed which includes the processing routines for the ECG and accelerometer data. In addition, to provide cardiologists, apart from the value of the EGC parameters, with the ECG trace itself, a compression scheme has been included to decrease the amount of ECG data that need to be communicated from the IPP to the medical analysis and storage subsystem (MASS). The MASS is a server-based framework providing medical experts with visualization and analysis tools for effectively monitoring the captured data. The raw physiological readings and the analysis outcomes are communicated to the MASS from the IPP through FTP protocol over wireless 3G data connection. This choice was dictated by the fact that 3G offers much wider coverage than any other wireless standard, allowing for data transmission to be taking place without the need of the patient being constrained to a specific area. To provide cardiologists with the ability to monitor the patient's status "anytime" a second Java-Android application (mIPP) which connects to the MASS and upon request downloads data and displays them in a handheld device (tablet/smartphone) was built.

Based on the above architecture, two operational modes were defined. In the real-time streaming mode, data are transmitted to the IPP in real-time while the processing outcomes are uploaded on the MASS at the moment of their production. Data and medical parameters are then accessed from medical experts with minimum latency. Under this mode, clinicians obtain a real-time assessment of the patient.

Although energy demanding, due to the continuous BT transmission, the real-time mode is ideal for patients in high risk of an impending episode or in situations where the clinician wishes to perform a remote stress test, by instructing the patient to walk on a treadmill while monitored. The second operational mode is the one expected to be utilized under normal conditions. In this mode, sensor data are not transmitted to the IPP in real-time. Instead, data are time stamped and locally stored to the communication modules during sensing. Once sensing is completed data transmission and processing on the IPP takes place in batch mode. The final outcomes are then uploaded and stored to the MASS. Medical experts can then access data through queries at will and thanks to timestamping, correlate and combine readings and outcomes obtained from different sensors. The IPP governs which operational mode is in use by commands issued to the sensor modules, which upon request can set their mode of operation.

## 10.2.4   Sensor Components

The sensor modules utilized in the CHIRON sensor platform are based on the Shimmer WSN module. The standard Shimmer platform is based on a

T.I. MSP430F1611 microcontroller, which operates at a maximum frequency of 8 MHz and is equipped with 10 Kb RAM and 48 Kb of Flash. An 8-channel 12-bit A/D converter enables connectivity with various sensors (ECG, EEG, accel, gyro, etc...). Wireless communication is achieved either with class 2 BT (RN-42 module) or through IEEE 802.15.4 (T.I. CC2420 module.). The standard BT v2 was elected as the sensor modules communication standard. For storage purposes the Shimmer platform is equipped with an integrated 2GB microSD card which is used in normal operation mode to store sensor readings (Burns et al. 2010). The power supply is comprised of a 450 mAh rechargeable Li-ion battery. Finally the Shimmer platform is designed to be programmed with the open-source TinyOS operating system (Levis et al. 2005).

### 10.2.4.1 ECG Sensor

The standard Shimmer ECG platform uses four snap electrodes attached through wires and medical patches to the body. It was thus deemed to be too invasive for the long-term monitoring purposes of the CHIRON system. The Shimmer ECG module was redesigned by replacing the four snap electrodes with two dry electrodes that can be attached to a commercially available chest strap (i.e. Polar®, Adidas®) and provide a single ECG lead. The resulting solution, depicted in Fig. 10.7, is lightweight (~80 g) with minimal invasiveness without any need for skin preparation or adhesive gels.

An analog front end with high gain and low cut-off frequency is necessary to condition the raw ECG signal and remove the noise for digital conversion and processing. The Shimmer ECG board has a low power front-end data acquisition circuit, composed by analog amplifiers and filters able to reduce the artefacts of movement, respiration and muscle contraction and to reach the desired dynamic range. The frequency response is 0.05–150 Hz with an amplifier gain of 175. The collected analog signal is then sampled through an A/D converter with 12-bit resolution. The digitized data are then passed to the microcontroller (MSP430) for processing and storage through a USART serial connection bus.

It was determined that in order to extract all necessary medical parameters, the ECG signal must be sampled at a frequency of at least 500 Hz. The quality of the acquired ECG signal from the customized platform was evaluated in hospital bedside settings as well as during a marathon run. Additional experiments were performed and the ECG was captured by both the CHIRON ECG chest strap and the Holter ELA device (considered as the golden standard for ambulatory ECG)



**Fig. 10.7** The customized ECG sensor
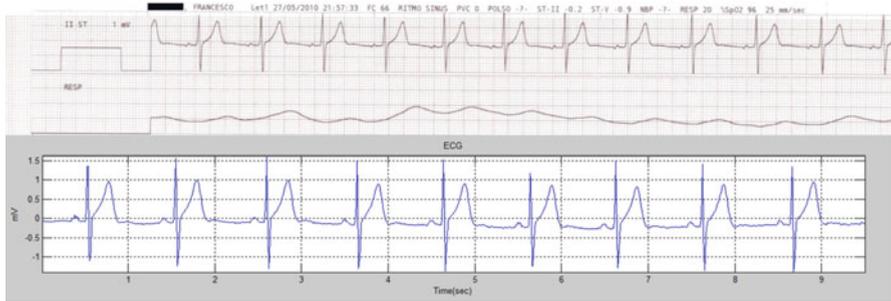
**Fig. 10.8** Comparison of ECG chest strap recordings with a standard ECG machine at bedside settings
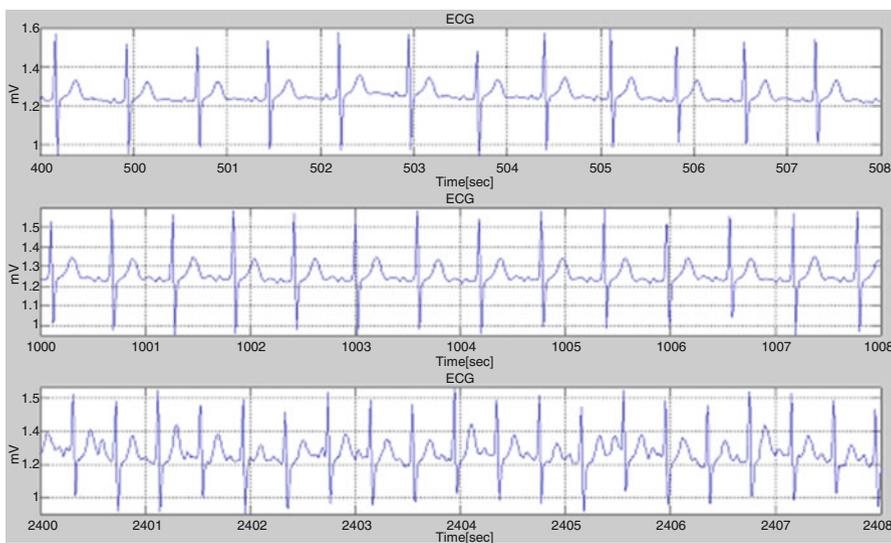


**Fig. 10.9** Three portions of ECG chest strap recordings of a runner during a marathon with different heart rates

simultaneously. The obtained waveform confirmed that the signal quality was comparable to the one acquired by the gold standard Holter. A comparison of bedside recordings demonstrated that the CHIRON chest strap recordings produce a similar waveform to the one captured by standard ECG machines as shown in Fig. 10.8.

The CHIRON ECG chest strap was also used to obtain the ECG of runners participating in a marathon. As depicted in Fig. 10.9 the ECG signal appears stable and with a negligible number of artifacts.

Additional tests were performed in five subjects having their ECG captured at bedside settings for 3 h using both the CHIRON ECG chest strap and the Holter
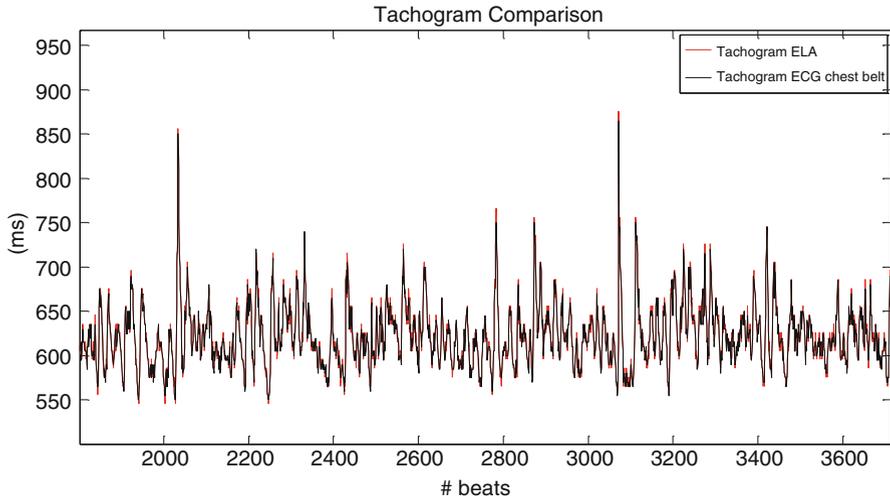
**Fig. 10.10** Comparison of the tachograms produces from the ECG chest strap and the ELA Holter

ELA. The ECG chest strap provided readable signal for more than 95 and 99 % of the time of acquisition while the subjects were working and lying supine at bedside respectively. Following, the ECG signals from both devices were analyzed and the heart rate (HR) of the subjects was derived from both devices. As it can be seen in Fig. 10.10, the two tachograms are almost identical and the low value of the mean error distribution, (~0.01 s), as depicted in Fig. 10.11 confirms the similarity of the ECG signals acquired by the two devices. In addition, this investigation justifies the ability to derive medical important parameters from the CHIRON ECG chest strap with a similar level of accuracy as with golden standard devices.

### 10.2.4.2  Accelerometers

Accelerometers are utilized in the CHIRON system in order to provide the required data for activity recognition and metabolic energy calculation. Two Shimmer platforms, each containing a 3-axis accelerometer (Freescale MMA7361) are used in the CHIRON sensor platform. The two accelerometers are placed on the chest and the thigh. These positions were chosen based on the achieved activity recognition performance on preliminary tests (analyzed in Sect. 10.2.3). The sampling frequency for the accelerometers was set at 50 Hz.

### 10.2.4.3  Temperature/Sweat Index Sensor (TS)

Clinical specifications for skin temperature and sweating index measurements dictate not to use more than one patches for collecting both temperature and sweat index data. Subsequently, a sensor combining both capabilities was
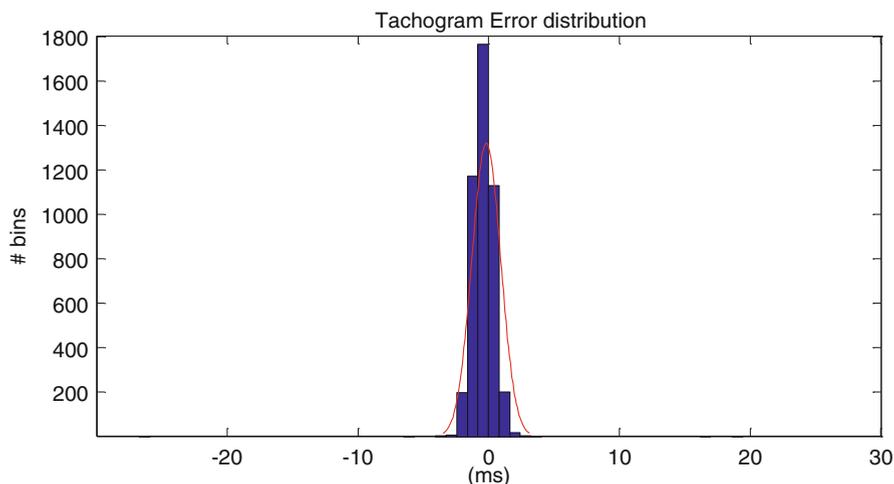
**Fig. 10.11** ECG chest strap tachogram error distribution with respect to Holter ELA

| Table 10.1 Temperature and sweat index sensor characteristics | Description | Value | Units |
|---|---|---|---|
| | Sensor size | $3 \times 3$ | mm$^2$ |
| | Active power consumption | 1 | mW |
| | Sleep power consumption | 1.2 | μW |
| | Humidity range | 0–100 | %RH |
| | Humidity accuracy | ±5 | %RH |
| | Humidity resolution | 0.04 | %RH |
| | Temperature range | 0–60 | °C |
| | Temperature accuracy | 0.3 | °C |
| | Temperature resolution | 0.04 | °C |

developed. The accuracy of the sensor should be better than ±0.5 °C error with a measurement rate of one temperature and sweat index sample per 5 min. In order to satisfy these specifications, the Sensirion SHT21 digital sensor was chosen (http://wwww.sensirion.com). This sensor is a suitable choice for temperature and sweat index measurements, as it integrates both a temperature and a humidity sensor, used to obtain sweat index data by measuring the relative skin humidity. The Sensirion SHT21 sensor is also suitable for the purposes of the CHIRON system in terms of size, accuracy and low-power consumption in both active and sleep mode. Table 10.1 summarizes the TS sensor characteristics.

The TS sensor is placed under the patient's armpit a common place for acquiring temperature and sweat index measurements (Sund-Levander et al. 2004). In the CHIRON system the TS sensor is connected to the Shimmer accelerometer module attached to the chest strap (through the I2C bus) as shown in Fig. 10.12. Temperature and sweating index values are sampled once every 5 min. Samples are
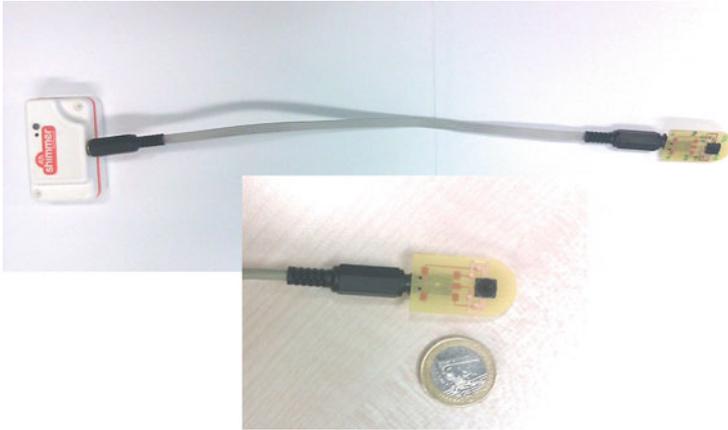
**Fig. 10.12** Prototype of the temp sweat index sensor connected to the Shimmer acceleration module

combined with the accelerometer data in a single message format and either stored or sent to the IPP. The platform was tested at a higher rate, i.e. every 20 s, in order to also check the autonomy of the sensor together with BT Shimmer module communications. Experiments were conducted with a volunteer wearing the sensor while performing different activities. Figure 10.13 shows the temperature and relative humidity of the volunteer who performed low physically demanding activities (e.g. sitting down or walking) until 7 p.m. when the volunteer changed to a moderate activity, (e.g. climbing stairs) for 15 min that resulted in sweating.

Results in Fig. 10.13 show a noticeable increment on humidity with a subsequent decrease when sweating stops. Concerning the results of the temperature, they are coherent with auxiliary temperature values and with temperature daily rhythms (Sund-Levander et al. 2002; Monk et al. 1995).

The sensor platform was also tested in a DYCOMETAL CCM81 climatic chamber with the chamber humidity being varied from 40 to 90 % in 2-h cycles for a period of 20 h while keeping the temperature constant at 36 °C. From Fig. 10.14, it is clear that the sensor follows the humidity variations almost instantaneously. This experiment also reveals that the autonomy of the platform exceeds 20 h at 20 s sample rate.

#### 10.2.4.4 System Integration

Modules Packaging

The four sensor modules were packaged into a single wearable system. The POLAR chest belt was used and customized to provide encapsulation for both the ECG module and the combined ATS module placed on the chest. Also the two Shimmer
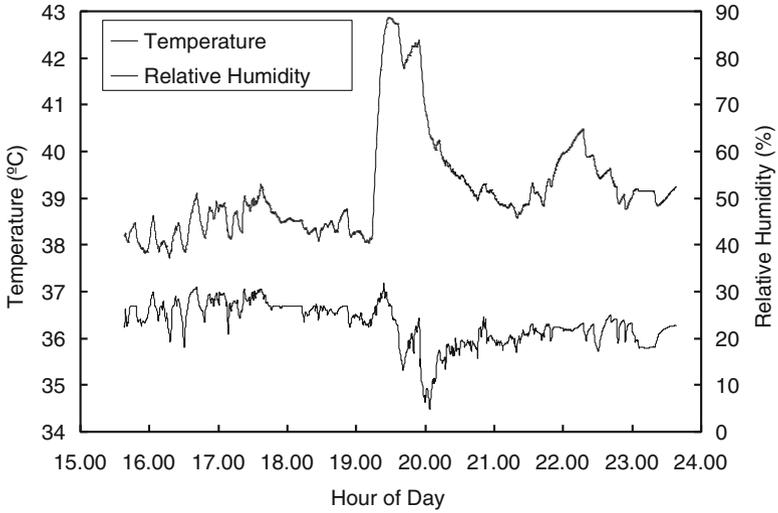
**Fig. 10.13** Skin temperature and relative humidity (sweat index) results for 8 h of continuous monitoring and for different physically demanding activities
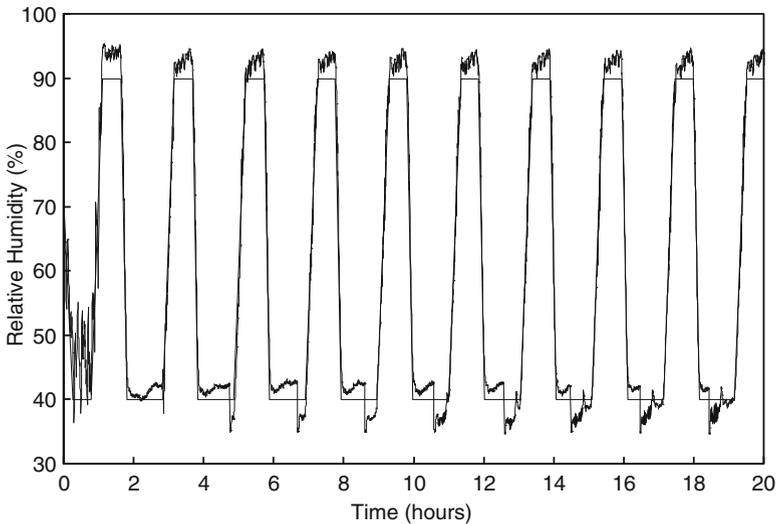


**Fig. 10.14** Sensor test for 20 h of continuous data acquisition. The humidity varies from 40 to 90 % in 2-h cycles while the temperature is kept constant at 36 °C

modules in the chest belt had their charging ports connected so the user can recharge them without removing them from their encapsulation. Figure 10.15 illustrates the enclosure of the two sensor modules and the placement of the strap on the lower thorax area. The ECG module and the ATS module weight, 28 and

**Fig. 10.15** The chest strap encapsulating the sensor modules

22 g respectively. The overall weight of the chest strap is less than 100 g, resulting in a non-invasive lightweight solution.

Firmware Development: Operational Protocol

To achieve the dual-mode functionality, imposed by the clinical requirements, all three Shimmer modules were programmed with both the ability to store sensor readings in their SD-card (with the BT turned off) or stream the readings through BT to the IPP. The user operational protocol was designed with two things in mind. The first was to minimize, as much as possible, the actions needed to be performed by the user and secondly to provide an energy-efficient strategy that would ensure a smooth uninterrupted operation. Subsequently the operational protocol was formed as following. Initially the sensor platforms are being charged on their docking stations with the BT "on" awaiting commands from the IPP. The required BT pairing of sensor modules to the IPP has taken place before the deployment of the system. The user removes the platforms and places them on his/her body to begin sensing.

Following the IPP sets the mode of operation to real-time and performs a sanity check on the correctness of the sensor placement. If this check fails the user is instructed to reposition the sensors appropriately. Once the IPP recognizes that the

sensors are correctly placed, broadcasts a command with the current IPP time to all modules to swap to normal operation mode. The sensor modules then turn the BT radio "off" and start logging data in their SD card. Once the logging period is over the user places the platforms at the docking stations again and the platforms turn "on" their BT. At this point the IPP requests the log, from each sensor, which contains information on the size of stored data. Then the IPP requests the stored data samples which are transmitted in batch mode. During data transmission, the platforms battery is recharged and a new operational cycle begins the next time (e.g. following day) that sensing must take place.

The sensor platforms customized firmware was developed in the TinyOS operating system. For the ECG sensor and the thigh accelerometer the typical TinyOS sensor components and interfaces were used to develop the sensor's firmware. On the other hand, the functionality of the ATS module had to be implemented. The TS sensor was integrated in the Shimmer module and connected to the I2C bus of the MSP430 microcontroller. A TinyOS interface was built in the stack layer to receive the TS data when necessary. The firmware for the ATS module employs both the accelerometer and TS interfaces in different sampling times.

In order to minimise the overall power consumption of the sensor platforms the BT module was kept "off", apart from when data are transmitted to the IPP either in real-time mode or in batches from the SD-cards at the end of sensing during the normal-mode. Predefined external events and commands produced by the IPP and formulated as TinyOS commands were used in order to trigger the swap, from one mode of operation to the other, initiate sensing and communication and govern the overall operation of the sensing platforms. Figure 10.16 illustrates the block diagram of an operational cycle and the commands and events that are generated. Figure 10.17 shows an analytical flow chart of the firmware that was developed for the ATS sensor platform. The description of the commands is as following.

*Commands initiated by the IPP*:
- Real-time operation: The sensor platform sample data at various frequencies (depending on the sensor) and sends each sample to the IPP.
- Normal operation: Platform stops Real-time transmission and wait for the absolute real timestamp from the IPP. The timestamp is written at the beginning of each log file and used as a reference for reconstructing the timestamp of each data sample. Following, the sensor platform turns its BT off and start logging data. No communication link exists between the sensor platform and the IPP during the logging process.
- Is Log Available: The platform checks if the log file is available and sends the status to the IPP.
- Send Log: The platforms send the log file. First, the absolute timestamp is sent, and then the data samples
- Delete Log: Platform deletes the log file.
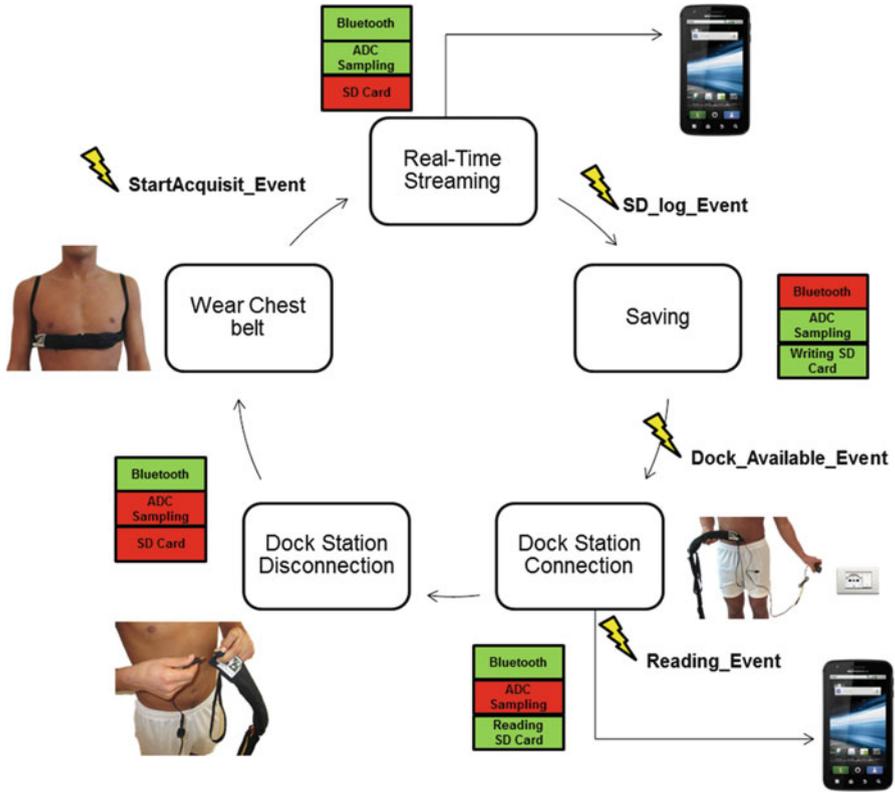
**Fig. 10.16** The operational cycle of the normal (SD-logging) mode of operation

*Sensor Event*:
- Docking event (the sensor is put on the charger after normal operation): The platform stops logging and turns on the BT. Yellow LED is turned on, indicating that the log file is ready to be sent.

Data Generation

Considering the Shimmer platforms specifications an analysis follows on the amount of data expected to be generated on a daily basis. Firstly, the MSP430 A/D channels perform 12-bit (2 bytes of storage) digitization and that a 16 bit (2 bytes) timestamp is stored for each sample, Table 10.2 summarizes our projections based on the sampling frequency of every sensor. Based on these calculations the total amount of data for 6–8 h of daily use should be 57.5–76.2 Mb. This amount of data does not pose any issue in any operational mode, since in the real-time scenario BT can achieve datarates up to 300 kbps
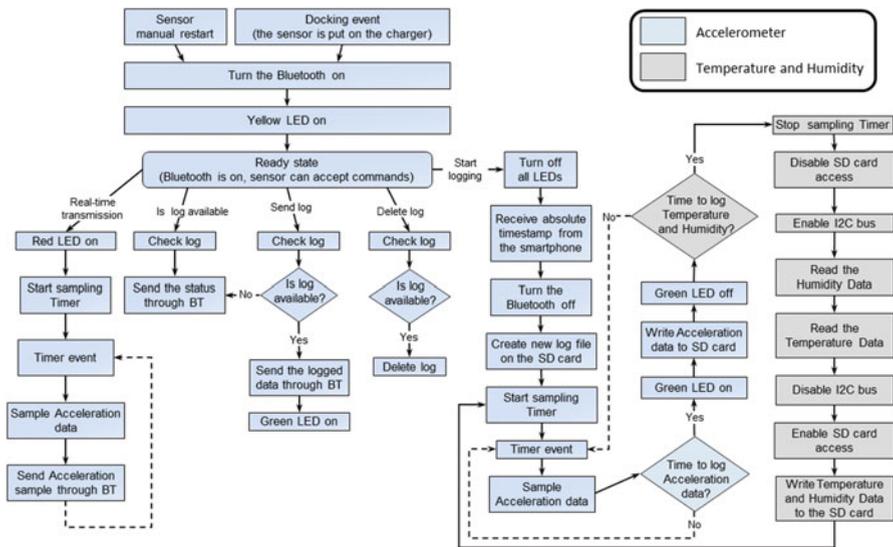
**Fig. 10.17** ATS platform firmware flow chart

**Table 10.2** Projected sensor data generation on a daily basis

| Sensor module | Sampling frequency (Hz) | Data per second (KB/s) | Data per hour (MB/h) |
|---|---|---|---|
| ECG | 500 | 1.95 | 6.85 |
| 2*Accelerometer (3-axis) | 50 | 0.78 | 2.74 |
| Temp/sweat index | 0.0033 | 0.0264 B/s | 0.0009 |
| Total | | 3.89 | 9.59 |

which is more than adequate for the amount of data generated per second and in the logging operating mode the micro-SD cards on the modules have more than enough capacity to store the generated data.

Energy Profiling

A crucial part, of the CHIRON system is to ensure that the energy consumption of the various system components is such, that under any mode of operation the clinical requirements are fully met. The energy consumption analysis of the Shimmer platform, presented in (Burns et al. 2010), designates the ECG to be the most energy demanding module in the SD-logging mode drawing an average of 4.5 mA at 500 Hz, compared to the accelerometer which draws 1.6 mA at 50 Hz. When the modules stream data in real-time through the BT the consumption increases to 21.1 and 15.9 mA for the ECG at 500 Hz and the accelerometer at 50 Hz, respectively.

**Table 10.3** Maximum battery lifetime for the three sensor components

| Sensor module | Maximum battery lifetime | |
|---|---|---|
| | Real-time mode | SD-logging mode |
| ECG | 8 h | 100 h (4 days) |
| Accelerometer | 18 h 30 m | 14 days |
| ATS module | – | 8 days |

The consumption of the T/H sensor is negligible since the Sensirion SHT21 sensor draws only 300 μA during operation and its sampling frequency is very small. The same analysis also states that an ECG module operating at 500 Hz can log data generated at the rate of Table 10.2, in the micro-SD card or stream them in real-time via BT for at least 48 and 12 h respectively considering a 280 mAh battery without any energy management protocol. From this analysis, it is safe to assume, that since the same hardware equipped with a 450 mAh battery is used the clinical requirement of 6–8 h data logging (in the storing mode) or an adequate amount of time (~1 h) for live streaming (streaming mode) can be easily met, provided that the module's batteries are fully charged at the beginning of sensing. Table 10.3 lists the maximum battery lifetime of the three sensors components as obtained from a series of experiments.

## 10.2.5 Information Processing Platform (IPP)

The IPP has a central role in the CHIRON monitoring system. Sensor data are fused in the IPP and processed accordingly. The IPP also governs the operation of the sensor modules and provides the user interface. It was decided that a latest generation Android-based smartphone would be the best selection for the IPP. Smartphones are universal devices with which users feel familiar. This is particularly useful since it will result in a small learning curve for both types of users. In addition, users normally carry smartphones almost all the time, which is ideal for the continuous monitoring scenario under consideration. Latest generation smartphones are equipped with powerful microprocessors and wireless connectivity chipsets which guarantee that the desired IPP operations can effectively run on such devices.

### 10.2.5.1 Analysis Algorithms

The data analysis algorithms comprise of the ECG analysis, which leads to the extraction of several medical parameters from the ECG signal and the activity recognition and metabolic energy calculation (ARMEC) algorithms, which use the accelerometer data as inputs. The temp/sweat-index data are not subjected to any processing and are simply fused to the MASS.
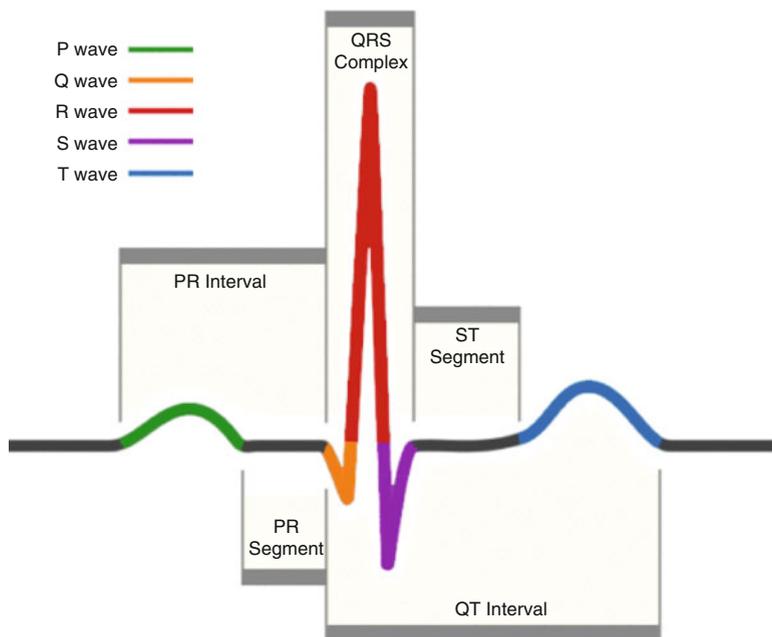
**Fig. 10.18** The ECG parameters

ECG Feature Extraction and Compression

For the ECG analysis the main demands are to provide clinicians with the required ECG-related parameters as well with the ECG waveform itself. Since the ECG provides a direct representation of the heart's electrical activity, cardiologists have defined a number of ECG parameters that are used for the evaluation of the heart's condition. These features are either morphological (e.g. R-height) or temporal (e.g. QRS-duration, QT-interval, ST-segment, etc). Figure 10.18 illustrates a typical PQRST-complex and the relevant ECG features. Evaluation takes place by examining the morphology of the waveform and the value of the clinically important parameters. For example, a prolonged QT-interval is a biomarker of arrhythmia, while an elongated QRS may be indicative of bundle branch block. The estimation of the aforementioned parameters requires the detection of a total of 11 time instances within a single ECG heartbeat (PQRST-complex). In details, the onset and offset instances of the P-wave, the QRS-complex and the T-wave, as well as the time instance of the peak of each wave (P, Q, R, S, T) must be extracted. By obtaining this set of 11 time points, all the relevant temporal ECG parameters can be calculated. Additionally, parameters defined between successive heartbeats (e.g. P-P interval, R-R interval) can also be approximated.

   A novel algorithmic solution, was subsequently developed which not only achieves the approximation of the ECG parameters with comparable to the state-

of-the-art accuracy, but also allows for an effective ECG compression scheme to be applied in parallel. This dual feat is achieved by employing the Haar Discrete Wavelet Transform (DWT) as the primary analysis tool. The DWT is realised as a cascaded filter bank using high and low pass filters defined according to the mother Wavelet and its scaling function. The output of the high pass filters provides the detailed coefficients (cD) and the output of the low pas filter the approximate coefficients (cA). The structure is known as Mallat's algorithm and allows for multi-level DWT decomposition to be performed by using the cA coefficients of a level as the output to the next pair of filters. It is established that due to the nature of the Haar function, potential extrema points in the input signal, will be represented as zero-crossing points in the cD coefficients and deflection points will be mapped into extrema in the DWT coefficients. By considering a single PQRST-complex and within it, the boundaries of the ECG waves as deflection points and their peaks as local extrema points, DWT multilevel decomposition in the dyadic space is performed and by using the aforementioned principle temporal points of the constituent waves of the ECG and the temporal location of the peak of each wave was extracted. Analytical details and performance results of the HFEA algorithm that was developed specifically for the CHIRON system can be found in (Mazomenos et al. 2013). The key novelty of the HFEA algorithm is the fact that it achieves comparable performance to the state-of-the-art ECG delineators while its computational complexity, in terms of mathematical operations required for its completion, is approximately five orders of magnitude smaller than that of the-state-of-the-art ECG delineators. It therefore provides an ideal solution for the continuous CVD monitoring nature of the CHIRON system.

Of all the ECG parameters (see Fig 10.18) the ST-segment (starting at the QRS-offset and finishing at the T-onset) carries significant clinical information and is of great value for the diagnosis of ischemic episodes and for the evaluation of the amount of oxygen supplied by the coronary arteries to the myocardium. Therefore, following the cardiologists guidelines, the ST-segment after being localised by the HFEA was subjected to additional processing for the calculation of a number of specific ST-segment medical parameters. Namely the ST-slope, the slope of the line connecting QRSoff and Ton points, the ST-deviation, the amplitude deviation of the ST-segment from the isoelectric line, the ST-area1, the area under the ECG waveform between the two ST-segment temporal boundaries when considering the isoelectric line as reference and the ST-area2, the area under the ECG waveform between the ST-segment temporal boundaries when considering the ST-line (line connecting QRSoff and Ton) as a reference were calculated using the Simpson rule. In total 20 ECG parameters are produced from the HFEA and the ST-analysis routines per heartbeat. These are either stored on the SD-card of the ECG module or transmitted directly to the IPP depending on the operational mode.

Finally the raw ECG data are also stored/transmitted in a compressed form. As analysed in Sect. 10.2.2 the majority of the generated data will be a result of the high sampling frequency (500 Hz) of the ECG Sensor. Moreover the clinical requirements dictate that clinicians must have access to the full ECG waveform apart from the value of the ECG parameters. This posed a requirement for an

efficient compression technique to be implemented alongside the HFEA algorithm. Since the DWT is utilized in the HFEA the inherent ability of DWT for compression and reconstruction of non-stationary signals was also exploited. Compression is achieved inherently in DWT because the frequency spectrum of the original signal is halved after each level of the DWT filter bank. Subsequently the output of the high and low-pass filters is subsampled, by a factor of 2 which discards half of the samples of the input signal and eliminates redundancy. Combined with a thresholding technique, based on the investigation of the Energy Packing Efficiency (EPE) of the resulting DWT coefficients, the compression scheme used in the CHIRON system maintains and store only those DWT coefficients that have a significant contribution to the energy of the signal. This is achieved by storing only the coefficients that have higher amplitude than a percentage of the maximum coefficient at that level. Reconstruction is achieved in a similar way that DWT decomposes the signal in cA and cD coefficients. The inverse DWT (IDWT) can reconstruct the signal from cA and cD coefficients using synthesis filters. Previous work reveals that the aforementioned compression method can achieve compression ratios of 16.5:1 and a percentage root mean square difference of 0.75 (Biswas et al. 2012).

Activity Recognition and Metabolic Energy Calculation (ARMEC)

The Activity Recognition and Metabolic Energy Calculation subsystem recognizes basic activities and estimates the patient's energy expenditure. To develop and test these methods, recordings of physiological signals during activities with different energy expenditures were made. The recordings consisted of acceleration, heart rate and skin temperature data used for activity recognition and energy expenditure estimation. Reference energy expenditure was provided by indirect calorimetry, and true activities were labelled by an observer. The reference energy expenditure was measured by Cosmed K4b portable gas analyser (http://www.cosmed.it/index. php?option=com_content&view=article&id=249&Itemid=174&lang=en), which computes the metabolic activity through the analysis of inhaled and exhaled gases. The recordings were made by ten subjects performing the basic activities to be recognized as listed in Table 10.4. The energy expenditure values are expressed in MET (metabolic equivalent of task, 1 MET corresponds to the average energy expenditure at rest), and are averaged over all ten test subject to provide an indication of the mean energy expenditure of each activity. Both the activity recognition and energy expenditure calculation were essentially tackled in the same way. The stream of acceleration measurements was split into windows, each window overlapping with the previous one by one half of its length. Several attributes were computed from the acceleration data within each window. These attributes formed a vector, which was fed into a machine learning algorithm. The algorithm constructed a model which either recognized the activity within the window or estimated the energy expenditure based on the average energy

**Table 10.4** Activities in the test scenario

| Activity | Basic | Energy (MET) |
| --- | --- | --- |
| Lying | Y | 1.19 |
| Sitting | Y | 1.26 |
| Standing | Y | 1.26 |
| Walking | Y | |
|    Slowly (4 km/h) | | 3.50 |
|    Quickly (6 km/h) | | 5.03 |
| Running slowly (8 km/h) | Y | 7.80 |
| Stationary cycling | Y | |
|    Lightly (1 W/kg of body mass) | | 4.91 |
|    Vigorously (1 W/kg of body mass) | | 7.22 |
| Kneeling | Y | 1.30 |
| On all fours | Y | 1.77 |
| Lying doing light exercise | | 1.28 |
| Sitting doing light activities | | 2.30 |
| Walking doing light chores | | 2.30 |
| Scrubbing the floor | | 2.65 |
| Shoveling snow, digging | | 3.40 |

expenditure of Table 10.4. The output of the activity recognition model was the used as input to the energy expenditure estimation model.

To reduce the number of attributes thus the computational complexity and power consumption, attribute selection was applied to the attribute sets of each of the two models. First, the quality of all the attributes was estimated using the ReliefF method (Kononenko 1994). The attributes were then ranked by their ReliefF score. Second, the attributes were removed from the attribute set one-by-one, starting with the lowest-ranked one. After each attribute was removed, the classification/regression accuracy was tested using cross-validation. The removal of low-ranked attributes slightly increased the accuracy, then the accuracy plateaued, and finally the removal of high-ranked attributes decreased the accuracy. The final attribute set consisted only of the attributes whose removal decreased the accuracy. The models were tested using the leave-one-person-out method. This means that the model was trained (including attribute selection) on nine test subjects and tested on the tenth. The procedure was repeated ten times, using a different subject for testing each time. This procedure estimates the performance on a previously unseen person.

A. Activity Recognition

Since the user's activity is changing over time, it should be recognized with an appropriate frequency. Prior work demonstrated that 2 s windows are a reasonable trade-off between the overall recognition accuracy (increases with window length) and the ability to recognize very short activities (decreases with window length), so considering the 50 Hz sampling frequency of the two accelerometers each window contains approximately 100 acceleration measurements (Žbogar et al. 2012).

From these, 128 attributes per window were computed, drawn from previous works (Gjoreski 2011; Tapia 2008). Attribute selection using the RelieF method reduced the number of attributes to 41. The attributes were computed from data processed by either a low-pass filter (to single out the acceleration component related to the user's posture, which changes infrequently) or a band-pass filter (to single out the acceleration component related to the user's motion, whose frequency is above the frequency of posture changes and below the frequency of sensor noise).

Prior work on activity recognition with accelerometer data showed that the Random Forest algorithm is the most suitable for this task (Gjoreski 2011). The attributes were thus used to train and test a Random Forest activity-recognition model, using the Weka machine. With the reduced attribute set (41 attributes), the classification accuracy was 92.0 %, which was a 0.8 % point increase compared to the full attribute set with 91.2 % classification accuracy. Although the difference in accuracy is not statistically significant, the computational complexity was reduced, due to both reducing the number of attributes in the model and by removing the calculation of attributes with complexity above linear in each window (energy, entropy, ...) which require the computation of Fourier transform. This improves the battery life and speeds up the recognition process.

B. Metabolic Energy Calculation

Since longer time is needed to estimate the energy expenditure, windows of 10 s were used (Luštrek et al. 2012). Each window contained approximately 500 acceleration measurements and 10 heart rate and 10 skin temperature measurements. For each window, 137 attributes were computed, 135 from accelerometer data, one was the heart rate and one the skin temperature. Attribute selection reduced the number of attributes to 29. Among these 29 attributes 5 require the calculation of Fourier transform, which was removed to decrease the computational complexity.

It was verified, through experimentation that the Support Vector Regression (SVR) algorithm, yields optimum results in estimating the energy expenditure estimation (Luštrek et al. 2012). Again the Weka framework was used to train and test the SVR model. The accuracy of the model in terms of mean absolute error (MEA) was 0.67 MET. The analysis of the error showed that the largest error occurred in the cases of running and cycling. To overcome this problem, two additional regression models were trained specifically for these two activities. This resulted in three regression models: two trained on running and cycling and used to estimate the energy expenditure on these two activities, and one trained on all activities and used on all activities except running and cycling (training on all activities increased the robustness in case running and cycling were misclassified by the activity-recognition model). All models were again trained with the SVR algorithm. The approach with three models resulted in MEA of 0.56 MET, a decrease of by 0.11 MET. Figure 10.19 illustrates the true vs. the estimated energy expenditures. On the x-axis are the true MET values and on the y-axis the estimated MET values.
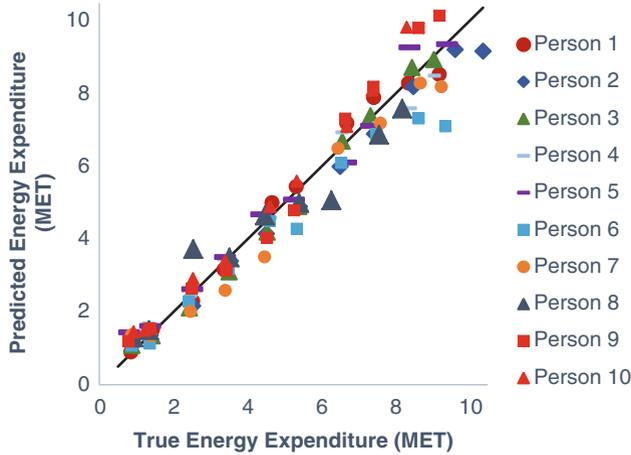
**Fig. 10.19** True vs. estimated energy expenditure

### 10.2.5.2 IPP Application

The IPP provides the user interface to both groups of users; medical experts and CVD patients. Subsequently two separate Android-based applications were developed that implement the functionality of the IPP for each user group—patient/user and medical experts.

Patient IPP (pIPP)

The IPP of the patient/user (pIPP) has the role of the gateway of the sensor plane analyzed previously. It is responsible for setting the desired mode of operation, synchronizing the data from the sensor modules, fusing the sensor data, executing the analysis algorithms and ultimately transferring outcomes and compressed data to the MASS. To implement these operations an Android-based application was developed and its overall architecture is given in Fig. 10.20.

To begin sensing, the patient attaches the two straps (chest and thigh) to his/her body, and initiates the system by pressing the "start sensing" button on the pIPP. The pIPP establishes communication with the three sensor modules through BT and depending on the mode of operation acquires the sensor readings either in real-time or off-line, from the Shimmer modules SD-card at the end of sensing. Latest BT modules attached on Android smartphones are more than capable of simultaneously maintaining the link and communicating to multiple BT modules. The pIPP sets the appropriate operational mode by transmitting commands through the BT link to the sensor modules. The core of the pIPP contains the two analysis packages of the ECG and ARMEC, both implemented in Java language as per the Android OS
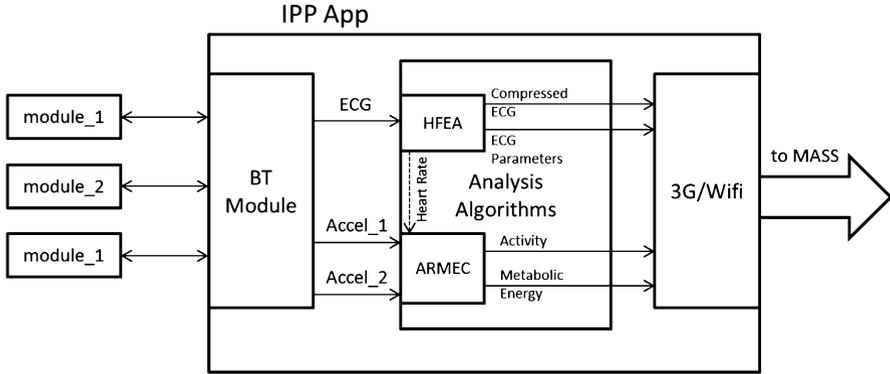
**Fig. 10.20** Schematic diagram of the IPP-app

requirements. Again the operational mode dictates the execution of the two algorithms either in real-time or off-line. Moreover the IPP-App is also tasked with conveying the algorithm's outcomes to the MASS through 3G wireless communications.

The analysis algorithms are also used to evaluate the quality of the received data and affirm the correct placement of the sensor modules before the beginning of sensing. This sanity check stage takes place in the pIPP, after the patient "starts sensing", by setting the system in real-time operation and evaluating the algorithm's outcomes. The patient is instructed to lie down for 30 s and then stand for another 30 s in order to confirm the output of the activity recognition subsystem. The ECG signal is evaluated by investigating the soundness of the HFEA results for 2 min. If one of the modules is found to be misplaced the user is then instructed to reattach it.

The pIPP uses the smartphone's real-time clock to inform the patient when monitoring must stop. In addition the pIPP is tasked with synchronizing the data received from the three sensor modules. Synchronization is critical as the ARMEC algorithms require the data from the two accelerometers to be synchronized. In addition, data synchronization facilitates the correlation analysis of different physiological parameters to take place (ECG parameters, activity) a requirement posed by the medical experts. Synchronization is achieved achieved using the "start sensing" command as reference and the Shimmer counter timestamp stored with every data sample. Each data sample is then labelled with a global timestamp by the IPP. This method will of course suffer from the inaccuracy of the Shimmer internal crystal clock (Epson FC-135 32.7680KA-A3) which has a tolerance of $\pm 20$ ppm, which results in 1.8 s maximal drift in 24 h. In the worst case scenario, when two sensors have different drift directions, the time difference is 3.6 s. However, in the CHIRON system a maximum of 6 h continuous logging is expected, which would result in a maximum drift of 0.9 s, which is acceptable for the task of activity recognition and energy expenditure. Experiments carried out showed that no

significant drift was present after 6 h and a time difference of 0.3 s was observed
among the two accelerometers after 24 h of continuous logging.

The user interface of the pIPP was designed in such a way as to require minimum
intervention from the user. In essence the user need to simply click the "START"
and the pIPP takes over and instructs the user to go through the sanity check and
then the normal sensing session begins. Moreover, the pIPP offers a report interface
where the patient/user can manually input the value of a number of medical
parameters (blood pressure, weight, etc..) not measured by the CHIRON system.
An illustration of the pIPP user interface is provided in Fig. 10.21.

**Fig. 10.22** The interface of the mIPP application; (**a**) ECG analysis (**b**) ARMEC analysis

Medical Expert IPP (mIPP)

The Android-based application designed for the medical expert user of the CHIRON system constitutes a monitoring interface in which medical experts can obtain the values of all parameters, measured by the sensors or produced from the analysis of the physiological signals. Data and algorithmic outcomes are first transferred to the MASS and the mIPP either obtains these with minimum latency if the system is operating in real-time mode or on a query-based approach where the expert specifies the time window to obtain data for. Figure 10.22 shows an example of the mIPP where the ECG analysis and the ARMEC analysis take place in the medical expert's handheld device.

### 10.2.6  Medical Analysis and Storage Subsystem (MASS)

The MASS is in essence a server-type database that receives data, through an ftp link from the pIPP. In the normal mode of operation, data are stored locally on the
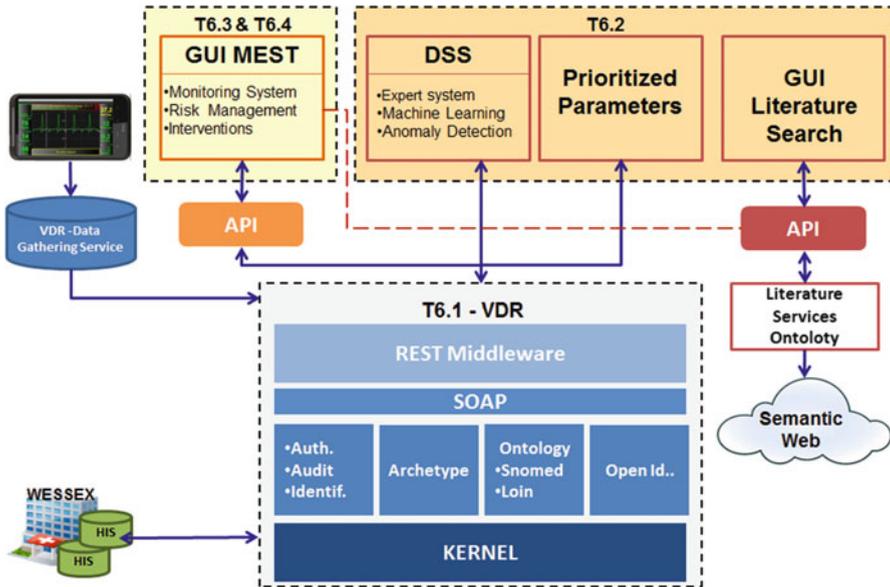
**Fig. 10.23** CHIRON integration of multisource information

MASS and upon a request from the mIPP, data that correspond to the specific timeframe, defined by the expert, are sent to the mIPP. In the real-time mode data are directly fused to the mIPP from the database with minimum latency. In addition to the mIPP, a web-based interface (Medical Expert Support Tool) was built on the top of the MASS to provide doctor with an enhanced tool for the monitoring of patients through the CHIRON system. In addition the MASS was built in such a way to facilitate the integration of multisource medical information and the analysis and feedbacks generation. Under CHIRON specialized software was developed to analyze and integrate all medical data obtained from heterogeneous sources (CHIRON sensor platform, imaging systems, laboratory values, epidemiologic data, lifestyle information, family history, etc.) and the data already existing in the Hospital System (HIS).

In the core of the MASS, the Virtual Data Repository (VDR) (see Sect. 10.2.6.1) provides an archetype-based solution to represent patients' Electronic Health Records (EHR). As represented in components integration schema, VDR is commonly accessed by all the other component of the MASS. All the flow of information is done through the VDR accepting and delivering data in several standards. Figure 10.23 illustrates the overall architecture of the MASS.

The integration done during the CHIRON project has followed several steps:

1. All the information is accessed using archetypes, but other standards are available (for instance HL7 CDA).
2. Decision Support systems are communicated with the Advance or Slim Medical Expert Support Tool (MEST) Graphical User Interface.

3. DSS communicates with the VDR directly. Once a day the three modules compute all the parameters stored in the database.
4. Retrieve the risk assessment values stored and the value of the parameters. The DSS component gives the results and writes them in the VDR using the archetypes.
5. An average of the parameters extracted from the raw data information coming from the tele-monitoring (VDR Gathering service) should be stored once a session (three sessions a day) in order to provide to the doctors a general view of the health status of the patient.

The information inside the archetype is retrieved by means of a GUID (Global Unique Identifier) which permits to identify each object. For CHIRON project the communication is done using RESTful web services through JSON which is compatible with the MEST UI (Fielding 2000). The VDR is accessed using a proprietary middleware (REST API).

### 10.2.6.1 Virtual Data Repository (VDR) Concept

Heterogeneous medical information comes from multiple systems. The Virtual Data Repository is the middleware, which permits the connection with the data management transparently for the user. The VDR covers all the storage components, the input to the modules of the system and will be the data on the patients, which will be gathered by the CHIRON sensor platform and contained in the patients' EHRs. However, data from other sources can also be included, for instance to train machine-learning classifiers and to demonstrate that the system works before the real data from CHF patients is available. The VDR is a set of repositories located somewhere and each element of the system could access to the data using the openEHR Kernel interface.

The VDR is physically in the hospital and has some very bright and clear aspects:

- It complies to the EU standard for medical data transport
- It has an interface model that "talks" all standardised languages (XML, Edifact, etc.)
- It can use the approved and authorized NHS Archetypes for this study
- It can connect to other Interfaces (like the Southampton General Hospital or Sapienza University Hospital).

### 10.2.6.2 Decision Support System

As mentioned previously, apart from the mIPP, with which the doctor is able to monitor the patient's physiological data, a more elaborate tool is required to provide doctors with the information and analysis mechanisms needed to make clinical

decisions regarding the patient. Therefore a web-based decision support system (DSS) was developed and linked to the VDR to accommodate this need.

The risk assessment component is divided into three sub-components using three different approaches. The expert system sub-component incorporates existing medical knowledge. The machine learning sub-component learns the relation between the parameters characterizing the patient's health and his/her risk using an Artificial Neural Network. The anomaly detection sub-component detects anomalies in the values and relations between the values of the parameters characterizing the patient's health, using the "Local Outlier Factor algorithm" (Barca et al. 2012). The literature search component is used when a doctor wishes to consult the medical literature on any issue that comes up during his/her decision-making process. It chiefly accesses data sources external to the CHIRON system, but the search can be contextualized by information from the patients' EHRs. The prioritized parameters component attempts to identify the parameters important for the risk assessment, and interesting relations between them. It can thus provide suggestions for the configuration of the risk assessment.

### 10.2.6.3   VDR Bridge

The openEHR REST API offers a set of functions to store and retrieve the data. In order to facilitate the access to the rest of components (DSS, MEST, etc.) a Java VDR library has been implemented called VDR Bridge. The library is a set of functions, which allow storing and retrieving the data from the openEHR REST API, but instead of using the long paths, the inputs and outputs are translated into meaningful clinical concepts. Figure 10.24 shows a snapshot of the main functionalities of the Java Library.

For the CHIRON Project several archetypes have been created or reused to cover 67 medical parameters in order to store the information in the VDR. The modified OBSERVATION archetypes have been used to retrieve the information (coming from the Monitoring Settings component). The CHIRON data is coming from the sensors and is retrieved using the archetypes included as entries inside one composition of the patient EHR. For each parameter OBSERVATION and EVALUATION archetypes downloaded from the CKM (see Chaps. 6 and 8 for further details) or created ad-hoc have been used to show the measurements, diseases, medications and so on.

The way to configure the clinical concepts and the archetypes is using the openEHR configurator dragging and dropping the paths read from the archetypes. This tool allows the user associating the parameters needed by the doctors to the archetypes stored in the openEHR kernel. The Graphical User Interface read the configuration file and builds the screens dynamically. Figure 10.25 shows an example of concepts and archetypes.
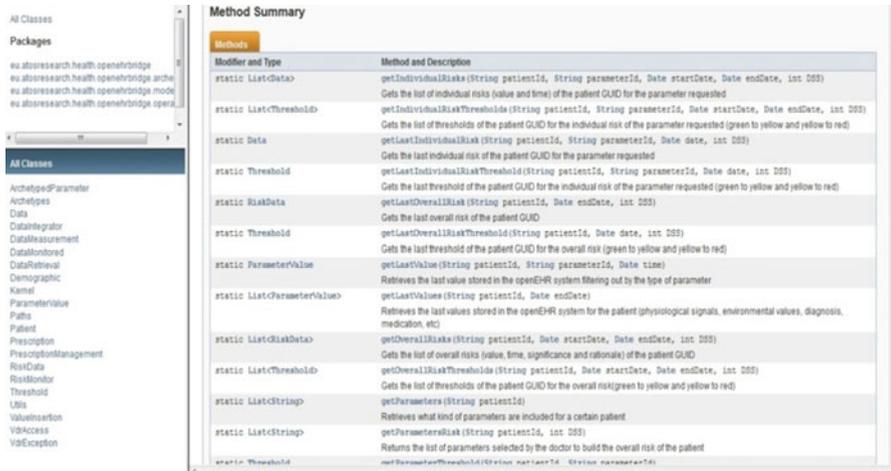
**Fig. 10.24**  VDR bridge API doc
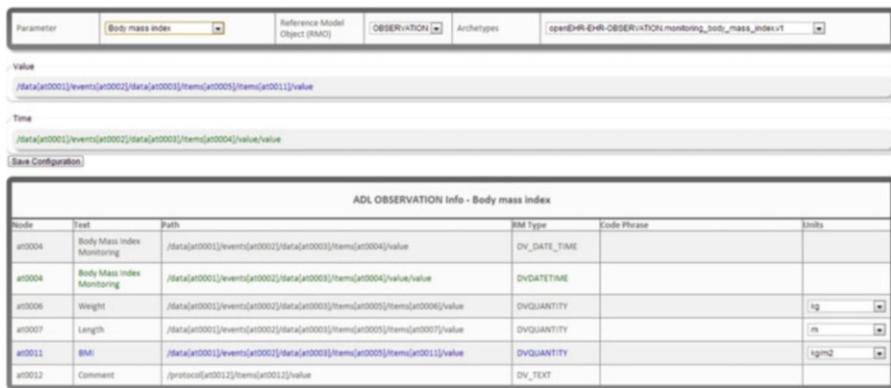


**Fig. 10.25**  openEHR configurator

#### 10.2.6.4   Medical Expert Support Tool (MEST)

Advanced MEST

"The Medical Expert Support Tools (MEST) is a set of UI-based tools built on top of Computer Based Clinical Decision Support System (CDSS). They have the purpose of helping the medical professionals to detect risk from chronic disease monitoring and subsequently to manage the risk in terms of assessment and intervention to mitigate the dangerous situation related to the detected risk factor" (Barca et al. 2012).
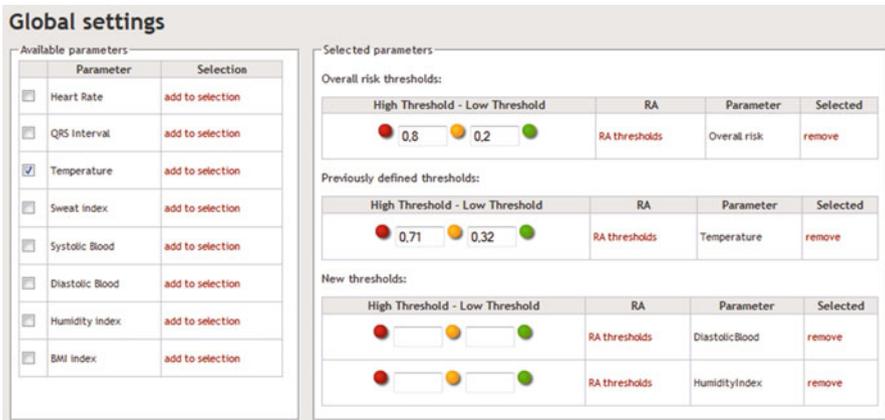
**Fig. 10.26** Monitoring settings GUI

The Advanced MEST provides the medical professionals with a multi-parametric view and an overall status of the patient indicating the risk factors with meaningful colours (green, yellow and red). The assessment of the person's risk based on the analysis of the information already stored in the system offers the doctor a clear insight of the current situation of the individual. The detection of critical situations will activate the feedbacks to the patient and to the clinicians. The MEST API is designed and developed as a RESTful API to communicate between MEST applications and adapt data from CHIRON backend services and components exchanging the clinical data.

The risk assessment procedure (Fig. 10.26) starts when the clinician configures the system communicating to the CDSS modules which parameters have to be measured and their corresponding thresholds.

Once the system is configured MEST presents the list of his/her patients with the overall risk coming from the CDSS components and stored in the VDR (see Fig. 10.27). The overall risk is calculated taking into account all the computed parameters shown by means of a green/yellow/red mark.

For each parameter configured an individual assessment is calculated (see Fig. 10.28) to provide the doctors with the specific evaluation of the values producing the risk factor along with clinical literature articles related with the disease of the patient and his/her monitored clinical parameters (left down in Fig. 10.28).

Finally the clinician can access the causes (parameter values) that led to the evaluation of a risk factor, displaying the complete history of the monitored clinical parameters (see Fig. 10.29). The thresholds of the parameters are also shown in order to see if the values exceed the limits (above or below).
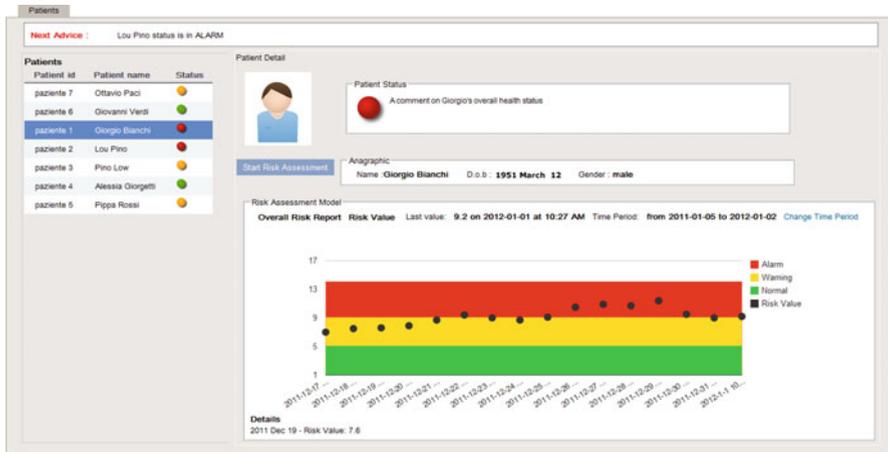
Fig. 10.27 Overall risk assessment view
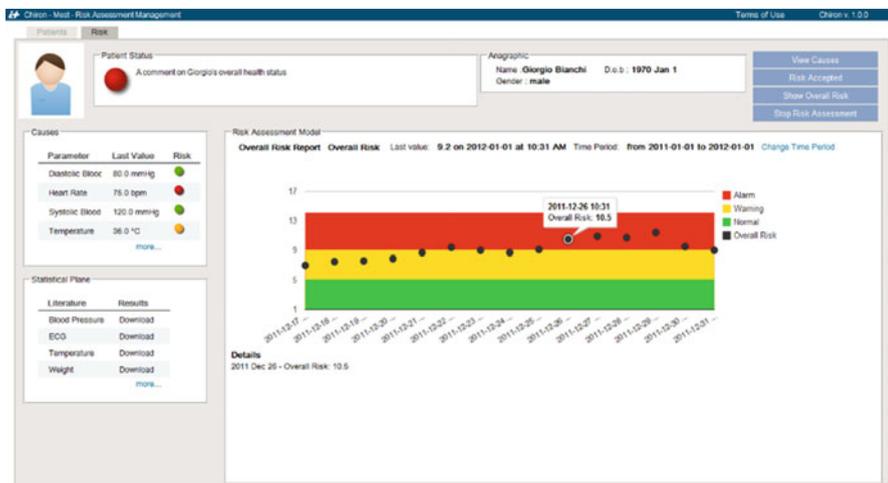


Fig. 10.28 Individual risk assessment view and articles contextualised to this patient

Refinement of Functional Aspects for Observational Study: Slim MEST

For the CHIRON Observational study the risk assessment modules were not included due to the lack of relevant data, which will be gathered during this period. For this reason clinical partners defined a new set of requirements focused mainly on Observational Study requisites enabling the medical user to insert whatever clinical data associated to a patient in openEHR format.

A new Graphical User Interface was proposed called "**Slim MEST**" which includes some parts of the MEST and allows the doctor to analyse the data of the
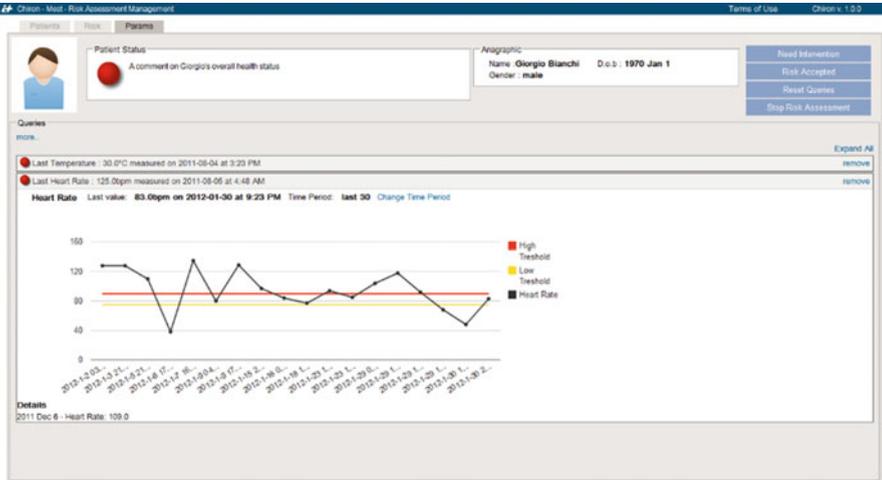
**Fig. 10.29** Clinical data and thresholds view

patient (monitored data) collected in the overall observation period plus some data generated by the doctor himself. The risk assessment is not included since the "rules" are still to be defined.

The **Slim MEST** includes:

- **Visualization of health status parameters**

  It shows the last health status of the patient coming from the sensors. After a correct access, main screen is loaded. The visualization option offers an overview of parameters that have been measured for selected patient. A period of time can be pre-selected both general and individual for each of the parameters. Data is displayed as a self-expandable table, which shows in every row parameter name beside its last value. Selecting one of the numeric parameters and choosing a period of time with different measurements produces a graph (Generate button) that illustrates parameter value variation. It is possible to generate a pdf file (Fig. 10.30).

- **Insert parameters health status**

  This option brings out a paginated list of all available parameters in CHIRON system. An empty text box lets the user update the value of each parameter. As a reference, last value stored is shown accompanied by the date when the measurement was taken. In case the user wants to repeat the value, a copy button provides this functionality. It will update the value with the current day and time. Controls section in the bottom of the page, lets the user:

    - Move back and forward between pages.
    - Print a PDF report with inserted values.
    - Store values.
    - Exit the insertion module (Fig. 10.31).
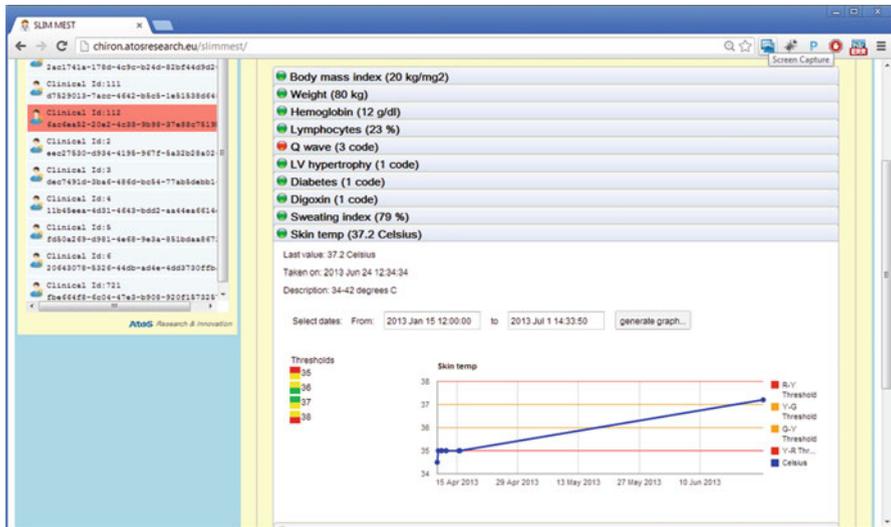
**Fig. 10.30** Slim MEST: visualization
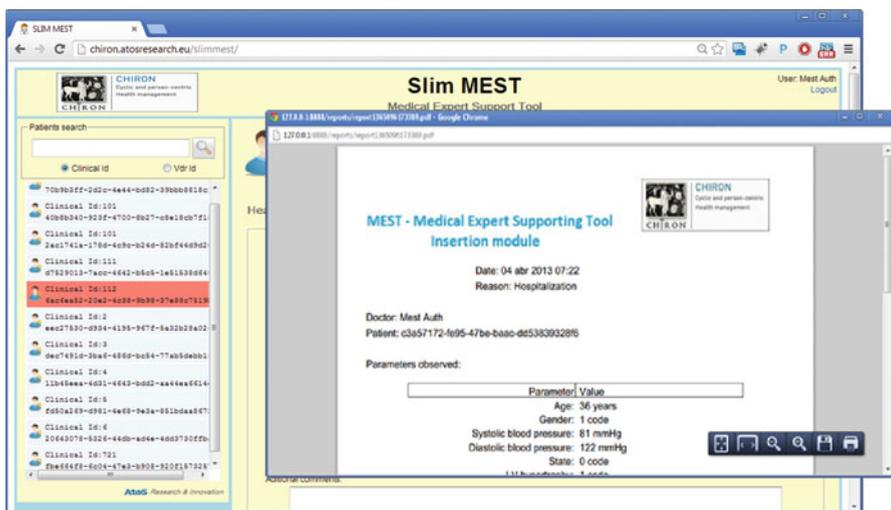


**Fig. 10.31** Last health status reports generation

*Security Aspects*

MEST has been designed to be embedded in a security system. From the point of view of the Graphical User Interface the main aspects to be considered are the authorization and authentication aspects. An authorization mechanism that allows the identification and access levelling of a caregiver is highly recommended, both

for security purposes and for privacy concerns. The REST services are designed to expect that the UIs add a textual (String) representation of an authorization token to every privacy-concerned (or potentially risky) action the user wishes to perform (e.g. request of the clinical data of a patient, or the notification of a risk acceptance). Slim MEST requires a Google account to get access to the tool (due to authentication process). Users that own a Google account can write their access details. The rest, can Sign up for a new account. After entering the system, the application asks for permission to access through your Google account. Accessing through Google API produces a token, which is required by VDR API which contains a list of medical users and patients associated to provide authorization.

### *10.2.7  Conclusions*

This chapter provided the reader with analytical details of the CHIRON Project case study. The CHIRON Project focused on combining state-of-the art technologies and innovative solutions into an integrated framework designed for an effective and person-centric health management along the complete care cycle of CVD. Within the areas of e-health and tele-medicine, the CHIRON case study proposed a holistic system architecture constituting of a wearable sensor system, its corresponding mobile application and an advanced interface for medical evaluation and analysis bundled into a single integrated framework for the continuous evaluation and assessment of CVD patients. To the best of the author's knowledge the CHIRON system is the very first attempt of an e-health tele-monitoring system towards the *Proactive Approach* for the care of CVD. The CHIRON system is envisioned as a tool to provide medical experts with the desired technological support for analyzing the variation and the correlation of heterogeneous medical data in an attempt to introduce novel biomarkers for the preemptive intervention in CVD.

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