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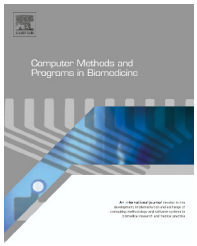

A generic telemedicine infrastructure for monitoring an artificial pancreas trial

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ABSTRACT

Telemedicine systems are seen as a possible solution for the remote monitoring of physiological parameters and can be particularly useful for chronic patients treated at home. Implementing those systems however has always required spending a great effort on the underlying infrastructure instead of focusing on the application cores as perceived by their users. This paper proposes an abstract unifying infrastructure for telemedicine services which is loosely based on the multi-agent paradigm. It provides the capability of transferring to the clinic any remotely acquired information, and possibly sending back updates to the patient. The infrastructure is a layered one, with the bottom layer acting at the data level and implemented in terms of a software library targeting a wide set of hardware devices. On top of this infrastructure several services can be written shaping the functionality of the telemedicine application while at the highest level, adhering to a simple agent model, it is possible to reuse those functional components porting the application to different platforms. The infrastructure has been successfully used for implementing a telemonitoring service for a randomized controlled study aimed at testing the effectiveness of the artificial pancreas as a treatment within the AP@home project funded by the European Union.

1. Introduction

Diabetes mellitus (DM) is a group of metabolic disorders featuring very high blood glucose levels (BGL) in individuals, which may be caused by defects in insulin secretion (Type 1 DM), in insulin action (Type 2 DM) or both [1]. Insulin is the principal hormone involved in the carbohydrates metabolism of the human body which enables fat cells to process blood glucose turning it into the lipid molecules representing their energy reservoir. Until recently DM treatment involved administering a small number of multiple daily insulin injections (MDII) according to the corresponding BGL readings taken just beforehand, although this approach caused wide BGL fluctuations across the day.

A major long term study carried out in the early 90s by the Diabetes Control and Complications Trial (DCCT) research group [2] proved that an intensive control over BGL is recommended for the diabetic patient's everyday life as it may substantially decrease and delay the risk of developing complications. The only way to achieve it is to provide patients with a pump continuously delivering insulin micro-boluses during the whole day as needed. The so called continuous subcutaneous insulin infusion (CSII) even predated the DCCT trial [3], although further improvements in pump miniaturization mechanics and in microelectronics addressing its control logic were needed before it was routinely adopted as a treatment. Nowadays CSII is being used as the primary way of administering an insulin treatment to diabetic patients and several studies are available in the literature demonstrating that it is

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safer, more effective and able to provide a higher quality of life with respect to traditional MDII treatments [4,5] also in children [6,7], while being at the same time more cost-effective [8].

CSII regimens are controlled through glucose readings occurring three to seven times per day, implementing what is known as a *partial closed-loop* scheme. Nevertheless, the latest advances in bio-technologies are opening up the possibility of continuous glucose monitoring (CGM) [9] thus anticipating a true *closed-loop* scheme. This control scheme replicates the process occurring in healthy individuals giving rise to what is known as the artificial pancreas (AP). Besides a CGM sensor and an insulin pump, the AP requires a controller as a core component for monitoring readings coming from the sensor and driving the pump in order to deliver insulin according to a suitable model of glucose absorption [10,11]. Preliminary tests have already been performed either *in silico* [12] as well as *in vivo* [13,14] with promising results foreseeing their applicability to ordinary human treatment on the short term.

In order to conduct further investigations on the AP pushing toward its final adoption as a routine treatment for DM patients, the European Union (EU) funded the AP@home consortium within the 7th Framework Programme with the twofold aim of first accomplishing an extensive tuning and validation of the insulin delivery algorithms and then proceeding with the implementation of an AP prototypical device. The first step involved setting up a multinational controlled trial involving 6 treatment sites spread all over Europe (Profil Institute for Metabolic Research GmbH in Neuss, Germany; Academic Medical Centre in Amsterdam, the Netherlands; Institute of Metabolic Science of the University of Cambridge, United Kingdom; Medical University of Graz, Austria; Department of Clinical and Experimental Medicine of the University of Padova, Italy and Endocrinology Department of the Centre Hospitalier Universitaire in Montpellier, France). The validation entailed enrolling 48 patients overall, with each one undergoing both *open-loop* and *closed-loop* sessions exploiting different algorithms during a 24 h time period. During that trial BGL levels, insulin boluses and any other information concerning a patient's state were collected in order to compare the performances of the therapeutic schemes. On those grounds we exploited a telemedicine (TMD) infrastructure designed within our research group for monitoring real-time physiological parameters acquired on patients [15], and adapted it for remotely following the outcomes of those experiments in real-time, with a twofold aim. On one side we enabled the researchers involved with the algorithm design within the AP@home project to watch in real-time the experiment outcomes over the patients despite the fact that their institutions were located far away from test sites. Nevertheless, at the same time we tested the whole architecture preparing for its final deployment which foresees patients undergoing closed-loop therapy for several days during which they will certainly need to be monitored by a specialist at some clinical practice.

We believe that the availability of a sound TMD infrastructure greatly helps in reporting to the clinic any information, concerning the AP treatment, acquired while the patient is busy with his everyday life. Such an infrastructure is beneficial either for supporting scientific trials or for educating the patient at the beginning of the AP therapy, or even for ensuring a careful monitoring throughout a patient's life [16]. Furthermore, if the design of the TMD infrastructure is carried out at a sufficiently abstract level it may also be applied to other chronic diseases enforcing the interoperability and reuse of its components. This results into a unified platform able to promptly detect any major problem on the short term, while extensive data analyses are carried out subsequently, helping in identifying dangerous trends and contributing to a better and more comprehensive treatment for the patient.

2. Background

Telemedicine applications exploit the information and communication technology (ICT) for bridging the gap existing between patients and the clinic staff and are often meant to support the remote provisioning of medical care in terms of diagnosis, treatment and consultations [17–19]. The potential for systems supporting the remote assessment of a patient's status and/or administering his therapy is enormous, and it is therefore no surprise that they have long been sought, with many attempts even predating the advent of the digital era [20–22]. However it has been only after the massive and cheap diffusion of the digital networks occurred during the 90s that those projects could get a head start for a promising deployment on a large scale impacting the population at large.

Remote care delivery for chronic diseases has always been a sensible topic since it improves the quality of life through the enforcement of a tighter control on health care policies [23] and it is presently becoming a must since it is believed to help in curbing the unprecedented demands on the national health care budgets faced nowadays by all developed countries [24,25]. Thus many applications have been addressing TMD support for chronic diseases and there is a common belief that the latest advances in ICT, yielding mobile smart-phones and miniaturized embedded devices, may further push the shift toward home care ensuring an independent living for chronically ill as well as for mobility impaired patients such as the elderly or disabled people [26].

DM due to its multi-disciplinary character encompassing both clinical and technological issues as well as patient empowerment is the chronic disease featuring the highest number of ICT applications, a huge part of which are addressing tele-monitoring [27]. This is probably due to the fact that a DM patient can experience an almost normal lifestyle inasmuch he is able to enforce a high level of control on his own therapeutic regimen. The very first remote monitoring of DM patient data happened through regular telephone consultations, yet proved a remarkable reduction of the hospitalization rates with the ensuing savings [28]. Disregarding that preliminary study, the first automated collection of data took place using modems for sending data acquired by glucose meters equipped with memory functions [29]. However it soon became clear that while the remote availability of BGL data at the clinic certainly simplified retrospective analysis, it had no impact in improving the therapeutic performance of the patient [30]. In order to succeed, BGL readings had to be complemented with additional information concerning the insulin boluses delivered, dietary data and even details of physical activity practiced by the patient, the acquisition of