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Human endocrine system modeling based on ontologies

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ABSTRACT

This article presents a novel use of an ontological approach of a rigorous generic model of the human endocrine system. It is based on an existing ontology specifically developed for chemical engineering design, named OntoCAPE. It provides most of the necessary concepts for implementing compartmental models of the human endocrine system, such as the UVa/Padova model,[1] accepted by the FDA.[2] We named this extended ontology Bio OntoCape which is connected with MatLab to perform dynamic simulation with the constructed model to predict the impact of the external stimuli such as meals intake and insulin dosage. This mathematical model was chosen because is enough versatile to represent healthy, prediabetic and diabetic persons. The complete system is thought to be helpful for participants from different disciplines, such as, endocrinologists, nutritionists, nurses, engineers and patients among others. In addition, it is envisioned that this development can be extended to configure an *e-Health* platform for diabetic patients treatment in Argentina. This will help to remotely monitoring patients reducing the personal attendance at hospitals as well as medical budgets.

1. Introduction

This work presents a first attempt to implement knowledge related to bioengineering study that centers the attention on diabetic patients treatment in the context of ontologies. Since an ontology is considered as *"an explicit specification of a conceptualization"* [9], it allows to represent consensual knowledge about a specific domain. Hence, ontologies represent a valuable tool for the ambitious project of constructing an e-Health platform for diabetes care. The focus of this article is to present an ontology-based modeling of the human endocrine system taking into account bioengineering elements.

For modeling the human endocrine system, we chose an existing ontology called OntoCAPE [16,18]. This decision was based taking into account the recommendations of the work of Bogle et al. [10] who emphasizes the potential role for Computer Aided Process Engineering (CAPE) in developing engineering analysis and design approaches to biological systems. The similarity between modeling chemical process and bio process and the availability of devices models such as sensors, valves, pumps, etc. and control algorithms too, were the main reasons for choosing OntoCAPE. It has been originally developed to support and simplify the development of software applications in CAPE, therefore, it is a good candidate to be extended to bio systems. We propose a customized knowledge-base from OntoCAPE, which contains the knowledge considered relevant for modeling compartmental models of the human endocrine system. We named this extension Bio OntoCape.

In the past few years, scientific community, mostly coming from medical domain, has involved many efforts and resources in the development of semantic technology. Legaz-García et al. [14] proposed semantic interoperability for using the valuable information of electronic health care records (EHR) data. Many web services platforms have been developed with the aim of assisting users with health information. One of these platforms is the Personalized Information Platform for Health and Life Services (PIPS) [2]. It combines a number of technologies in order to give advices to users. It is based on an ontological approach to achieve a common understanding of the domains in which the system operates. At work [1] a framework for diabetes education content management in accordance to semantic web concepts is described. The world wide web offers a wealth of information resources on diabetes mellitus that can answer most of the knowledge needs of clinicians and their patients. The aim of the project was to make

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[1] The UVa/Padova Type 1 Diabetes Mellitus Metabolic Simulator is a computer model of the human metabolic system based on the glucose-insulin dynamics in human subjects

[2] U.S. Food and Drug Administration

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medical web resources more meaningful to computers to reduce the risk of overloading patients and medical practitioners with unnecessary or low quality information. At work [19] is proposed to integrate multidimensional data warehousing with data mining tools and ontologies. This is because ontologically described multidimensional data warehouse and mining facilitates the knowledge extraction. Rajbh et al. [20] describes a Medical Information System based on semantic web technology for sharing data between different hospitals. The heterogeneous nature of the health care data makes it a very suitable candidate for Semantic Web Application. The knowledge-based telemonitoring platform described in [23] is another example of a remote health-care application. This health-monitoring system checks a patient health status using a smartphone. The knowledge-base design involved ontologies and various reasoning methods. All of these cited works constitute examples of the development of semantic web technologies for health care.

The modeling of knowledge using ontologies enables the interoperability needed by the *e-Health* platform for the assistance of diabetic patients. This platform would be used by different actors like doctors, nurses, endocrinologists, chemical engineers, computer science specialists and, of course, also the patients. The ontology will allow to overcome the problem associated to the usage of different terminology handled by the different actors that will use the platform. Search engines can then work on a particular concept rather than trying to find ambiguous keywords. In the particular case of the e-Health platform, this feature is very advantageous for a patient who wishes to inquire about his treatment. This would increase the involvement of the patient into his treatment that would impact in the quality of his life.

The platform aims to reduce the number of visits to the doctor. This would be a great benefit for patients with low resources as well as those patients with difficulties to follow any treatment. All ontologies that will be developed within the project must be created having in mind that they must be coupled together to improve the quantity and quality of knowledge about the treatment of a particular person or a group of people. To resume, ontologies provide a suitable inter-semantic framework for a diabetic patient through which he may have a better control over his treatment, his blood glucose levels and a better understanding of his body behavior, which will help to achieve a better quality of life.

2. Motivation

Diabetes mellitus is a chronic disease, which in recent years has become an epidemic. This disease shows up when the pancreas can not produce enough insulin (Diabetes mellitus type I - DMTI) or when the produced insulin does not have the necessary properties to be effective for a person's body (Diabetes mellitus type II - DMTII). The insulin is a hormone that allows to metabolize the glucose from ingested food for being then used by the body cells to produce the necessary energy for muscles and tissues.

According to the last *World Health Organization* (WHO) study of global burden of disease, diabetes is the 19th leading cause of disease burden, and it is expected to rise to the 10th position by the year 2030. In Latin America, the situation is also discouraging, diabetes is the 6th cause of disease burden. In Argentina, diabetes affects 9.6% of the adult population, being DMTII the most common (90%) clinical form [8].

Diabetes is an expensive disease in Argentina as well as worldwide and its prevalence is continuously rising, affecting the quality of life of people and their life expectancy. It also imposes a heavy burden to the argentinean health care budget and on the economy in the form of productivity losses [3]. Overall diabetes prevalence increased from 8.4% in 2005 to 9.6% in 2009 at national level. In 2009, diabetes was the 7th leading cause of death with a mortality rate of 19.2 per 100,000 habitants. The *per capita* hospitalization cost for people with diabetes was significantly higher than for people without the disease, US$ 1,628.- vs. US$ 833.- in 2004.

Mathematical modeling is now widely applied in physiology and medicine to support the life scientist and clinical worker . Our aim in writing this article is to provide an introduction to this topic, presenting the underlying principles of good modeling methodology together with specific example of the endocrine system based on the expert knowledge given at the book [4] which is very useful for diabetic patients. Mathematical modeling finds application in medical research, in education and in supporting clinical practice. In the research context, the use of models can, for example, yield quantitative insights into the manner in which physiological systems are controlled. In the educational setting, medical students can use computer model simulation to explore the dynamic effects of pathophysiological processes or of drug therapy. In the clinical area, mathematical models can enable estimates to be made of physiological parameters that are not directly measurable enabling predictions to be made as to how changes in drug therapy will impact on variables of clinical importance such as blood glucose concentration. This article could be of interest to a wide range of student and practitioner backgrounds. In terms of the student readership, it is designed to appeal to biomedical engineers and to others studying physical and engineering sciences, and biological and life sciences. It should also appeal to medical students who wish to enhance their quantitative understanding of the physical and chemical processes that shore up physiology and medicine. Further, this article should be of interest to practitioners of bioengineering who have an interest in quantitative aspects of physiology and medicine. This article is based on the exploration of some of the complexities of physiology involved in the human endocrine system and their quantitative features where the ontologies could help to be better understood. The concepts used here for constructing efficient mathematical models with the help of ontologies could be considered as a novel way to be used for a wide range of purposes: to gain insights, to support processes of measurement, to make predictions of future behavior and in a variety of ways assist in enhancing clinical research and practice. A number of approaches to developing mathematical models mainly based on first principles concepts are then considered, with each being illustrated by three examples. Ensuring that a mathematical model is valid; that is to say fit for its intended purpose. Hence, the objective here is to demonstrate, how to handle the modeling concepts, methods and techniques that are described and discussed here can be extended to other real-world problems in physiology and medicine. However, since the physiological modeling is very much an interdisciplinary subject, the topic is also central to a range of related disciplines including biomathematics, biochemical, medical and health informatics and systems physiology. The focus of this present article is the use of ontology to provide a comprehensive introduction to the modeling of dynamic, physiological endocrine systems. The emphasis is placed firmly on developing sound modeling methodology, with some examples included as illustrations. Then, to achieve our purpose we had into account that the most recently, ontological software engineering has developed into a scientific field of its own, which puts particular emphasis on the theoretical foundations of representation and reasoning, and on the methods and tools required for building ontology-based software applications in diverse domains. Though this field is largely dominated by computer science, we propose an interdisciplinary work to achieve close relationships to be established with its diverse areas of application. Hence, the researchers involved in this area are interested in exploiting the results of ontological software engineering, particularly to build large knowledge-intensive applications at high productivity and low maintenance effort firstly dedicated to the problem of diabetes care. We detected very