Towards the Adoption of Agent-Based Modelling and Simulation in Mobile Health Systems for the Self-Management of Chronic Diseases

Sara Montagna Andrea Omicini Francesco Degli Angeli Michele Donati
DISI–Università di Bologna
via Sacchi 3, 47521 Cesena, Italy
Email: {sara.montagna, andrea.omicini}@unibo.it

***Abstract*—The impact of mobile technologies on healthcare is particularly evident in the case of *self-management of chronic diseases*, where they can decrease spending and improve the patient quality of life. In this position paper we propose the adoption of *agent-based modelling* and *simulation* techniques as built-in tools to dynamically monitor patient health state and provide recommendations for self-management. To demonstrate the feasibility of our proposal we focus on Type 1 Diabetes Mellitus as our case study, and provide some preliminary simulation results.**

I. Introduction

The introduction of information and communication technologies into healthcare systems is revolutionising medicine. In particular, the emergence of *mobile things* connected to the Internet even while moving around – the Internet of Mobile Things (IoMT) [1] – is opening new frontiers in healthcare. This field is often called mobile Health [2], [3]—*m-Health*, in short: humans are typically equipped with wearable devices (such as smart watches, wrist bands, smartphones, etc.) that measure, store, transmit, and possibly also elaborate vital parameters of the person, providing specific information about individual's health state. M-Health is expected to have a big impact in healthcare, since it facilitates clinical data collection, access, sharing, and elaboration.

A specific issue in m-Health is the *self-management of chronic diseases*. Chronic diseases, such as diabetes, respiratory illnesses, and cardiovascular diseases, constitute the most common and costly health problems of our society: in 2013, the Pan American Health Organization (PAHO) in collaboration with the World Health Organization (WHO), estimated chronic diseases to consume a huge percentage of total health-care spending [4]. Also, they are an important source of disability, as they strongly impact the quality of life of patients with ad-hoc dieting, sport activity, regular treatments, social and work life adjustments, and significant emotional consequences.

To reduce the cost of health care systems and improve the quality of the patient daily life, an increasing number of interventions have been developed in the last years to transfer aspects of chronic illness control from the caregiver to the patients themselves. These are characterised by substantial responsibility taken by patients, and are commonly referred to as *self-management* interventions [5], [6]. M-health has a big potential in this context, mainly because mobile devices are commonly equipped with hardware and software technologies for real-time data acquisition, storage, sharing, and elaboration, thus enabling [7]:

- *healthcare professionals* to be continuously updated on the patients health by receiving data such as vital signs measures decreasing the occasions for patients to travel to health facilities;
- *patients* to be supported in daily decisions by instructions delivered by Personal Digital Assistant (PDA) applications that are based on the elaboration of these data.

In this paper we focus on candidate algorithms and computational technologies for the analysis and elaboration of patient data. While literature typically refers to technologies like big data, machine learning, and decision support systems [8], we here advocate the adoption of modelling and simulation techniques, and agent-based modelling and simulation (ABMS) in particular. We claim that the possibility of modelling how a complex system – such as the human body – evolves over time, is crucial for providing predictions of the health conditions of the patient in the near and far future. Such predictions are useful input for identifying a set of corrective actions the patient should take for a better health and to prevent disease exacerbation. Adopting ABMS as a tool associated to mobile devices could allow patients to monitor their own health state, and provide feedbacks driving them in their daily life.

The main objective of this work is to demonstrate the feasibility of our proposal. To this end, we present an agent-based model for self-management of Type 1 Diabetes Mellitus. Diabetes is a chronic disease that affects the physiological mechanisms controlling glucose concentration in the blood plasma. It occurs when the normal insulin-glucose-glucagon regulatory mechanism is affected, because either the pancreas does not release insulin (Type 1) or body cells do not properly use insulin to uptake glucose in the blood plasma (type 2) [9].

In the following we first motivate our work, analysing the role of IoMT for disease self-management, then present and evaluate our proposal with preliminary experiments showing the data-driven modelling of the dynamics of glucose, insulin, and glucagon in a healthy person and Type 1 DM patient.

II. IoMT and m-Health

IoMT holds promise to pave the way for a new era in medicine, changing the way health-services will be provided [3], [2], [10]: the adoption of mobile devices, equipped with sensors and internet connectivity, plays a key role enabling healthcare services to *anyone*, *anywhere*, and *anytime*, as from the definition of [11]: "Pervasive healthcare is the conceptual system of providing healthcare to anyone, at anytime, and anywhere by removing restraints of time and location while increasing both the coverage and the quality of healthcare".

A number of improvements are expected in healthcare by the introduction of IoMT:

- increasing *accessibility* of health-services, by guaranteeing a wider coverage; most in fact own a mobile device with which they can access diverse services devoted to improving their health, from the simplest cases of SMS reminders with dates of appointments, SMS or emails for communications from the health professionals, SMS or emails with medical reports, to the more complex cases of data acquisition (via sensors), transmission, and elaboration;
- decreasing the *cost* of healthcare, since people can avoid to frequently move towards healthcare facilities and, caregivers can be automatically updated in case of unexpected changes;
- supporting chronic disease *self-care*, by enabling data collection, sharing and disease tracking, to support diagnosis and personalised treatment —well turn to in more detail on that in the following;
- providing suitable tools for timely managing healthcare in *emergencies*.

III. Self-Management of Chronic Diseases

Self-management of chronic diseases is defined as the active involvement of patients in their treatment with day-to-day decisions about different actions to be taken: control of symptoms, take medicines, make lifestyle changes, undertake preventive actions. It is thus characterised by an extensive responsibility that the patients need to take on [6], [12]. Since the expected outcome of the patients self-management is to maintain a satisfactory quality of life, various initiatives are devoted to identifying how to support patients in their daily decisions, without leaving them alone, *i.e.*, guaranteeing health professionals intervention by automatically issuing emergency alarms.

IoMT technologies can significantly improve disease self-management [13], [14]. However, notwithstanding the explosive improvement of technology, which is crucial in data acquisition by built-in ad hoc sensors, data sharing, and patient interactions, there is a considerable lack of well-established models, theories, and algorithms capable of effectively supporting disease self-management in m-Health. Most of the available literature proposes algorithms and theories from computer science for elaborating data, such as complex event processing, data mining tools, big data technologies, machine learning, and decision support systems [8].

In this paper we propose the adoption of modelling and simulation tools that are gaining acceptance in medicine as a valuable support for decision making, since they provide both, short-term and long-term clinical predictions of patient health [15]. Such predictions provide information for making the most informed choices between available treatments and interventions. In particular, among the different simulation approaches, we here propose the adoption of the agent-based model (ABM).

A. Agent-Based Model

In the literature, agent-based systems, and MAS in particular, are considered an effective paradigm for modelling, understanding, and engineering *complex systems* [16], and biological systems in particular [17], since they provide a basic set of high-level abstractions that make it possible to directly capture and represent main aspects of complex systems, such as interaction, multiplicity and decentralisation of control, openness, and dynamism [18], [19], [20], [21].

In the pioneering work of Bonabeau [22], an ABM describes the system *from the perspective of its constituent units*. Moreover he states that:

> The benefits of ABM over other modeling techniques can be captured in three statements: *(i)* ABM captures emergent phenomena; *(ii)* ABM provides a natural description of a system; and *(iii)* ABM is flexible. Emergent phenomena result from the interactions of individual entities. By definition, they cannot be reduced to the systems parts: the whole is more than the sum of its parts because of the interactions between the parts. An emergent phenomenon can have properties that are decoupled from the properties of the part. [...] ABM is, by its very nature, the canonical approach to modeling emergent phenomena: in ABM, one models and simulates the behavior of the systems constituent units (the agents) and their interactions, capturing emergence from the bottom up when the simulation is run. [22]

This is why we consider ABM as a suitable approach for modelling the complex dynamics of disease physiopathology.

B. Self-Management System Model

We model the whole healthcare system as an agent-based system composed of two levels, as shown in Figure 1:

1) a *high-level model* that represents patients and their interactions with a tool supporting diabetes self-management, such as a PDA;
2) a *disease model* that represents the disease physiopathology and predicts the state of the patient in the near and far future.

The high-level model reproduces the behaviour of patients, and how they respond to feedback received through their personal devices. We assume that PDAs acquire *(1)* information from the individual about the composition of their meals, *(2)* information about individual physical activity from embedded

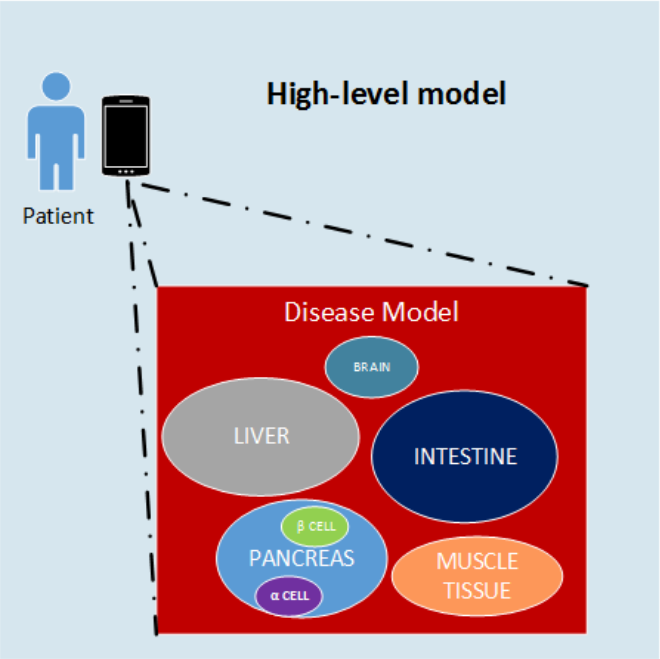


Figure 1. Two levels model of the self-management system

sensors, such as accelerometers, and finally *(3)* information about glycemia values, gathered wirelessly from a wearable device. These data are used as input for the chronic disease model. In the following we demonstrate the feasibility of our proposal by adopting Type 1 Diabetes Mellitus as our case study.

IV. Background on Type 1 Diabetes Mellitus Physiopathology

Diabetes mellitus, diabetes in short, is a chronic metabolic disorder characterised by an excessive amount of sugar circulating in the blood plasma, *i.e.*, *hyperglycaemia*, for a prolonged period. Diabetes is strictly related to *insulin* defects. Insulin is a hormone produced by the *β-cells* of the pancreas; it has a crucial role in the absorption of glucose in two-third of body cells, but mainly in fat, liver, and muscle cells, where glucose is a necessary source of energy for the cells to perform their activities. Diabetes is due to either an autoimmune process, where pancreatic β-cells do not produce enough insulin (Type 1 diabetes mellitus, Type 1 DM in short), or else the cells of the body develop a sort of "resistance" to insulin action, thus not responding properly to the insulin produced (Type 2 DM). In the following, we first describe the metabolic system, then how the physiological functions are affected by the lack of insulin, as in Type 1 DM.

A. Metabolic System

Every cell in our body needs fuel in order to fulfil its specific function. Glucose is the main source of such energy. It is obtained firstly from the food we eat (and drink, possibly) via the intestinal absorption, which ensures food to be broken down into the monosaccharide form of glucose that is then released into the blood. The blood flow ensures that glucose is delivered to all cells of our body. Finally, glucose diffuses from the blood into cells where it is used as an energy source via the aerobic respiration, or where it is stored as glycogen, a polysaccharide of glucose composed of varying numbers of glucose units, depending on the cell type (for instance, glycogen of muscle cells is composed of around 6.000 units of glucose, while liver cells require 30.000 units of glucose to create a glycogen molecule).

Plasma glucose levels are normally maintained within a narrow range ($70-100\ mg/dl$) through the combined antagonistic action of the two pancreatic hormones, *insulin* and *glucagon*, which enable the uptake and release of glucose from the blood into cells and vice-versa:

Insulin — It is a hypoglycaemic hormone, *i.e.*, it is responsible for enabling the uptake of glucose, mainly into fat and muscle cells, thus reducing the level of glucose in the blood. It is produced by pancreatic β-cells as a function of glucose concentration in the blood (formally called *glycaemia*): a basal secretion of insulin from β-cells is always observed, ensuring the availability of glucose at all times; instead, sinks of postprandial secretions are observed, *i.e.*, when the blood glucose levels are high. Secretions finally stop in case of hypoglycaemia.

Glucagon — It is a hyperglycaemic hormone that promotes the release of glucose from the liver cells into the blood. It is produced by pancreatic α-cells when glycaemia is low, normally in fast periods, such as during the night. Therefore, α-cells behave in the opposite way than β-cells: they have high secretion rates when the blood glucose concentrations are low, and low secretion rates when the glucose levels are high [9].

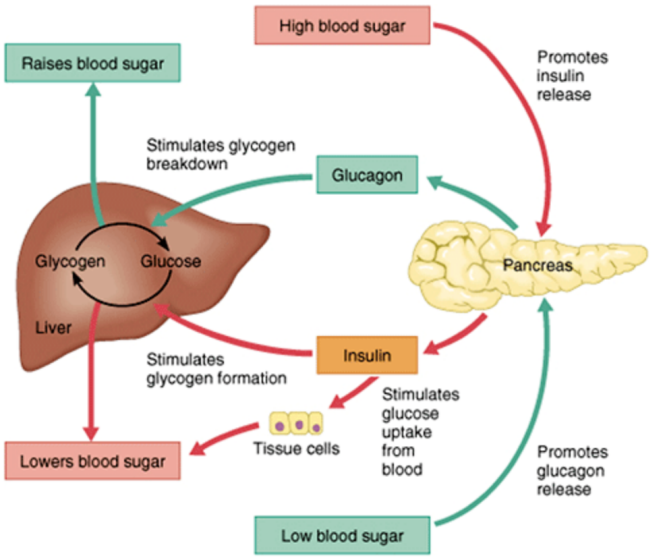


Figure 2. Metabolic system © 2001 Benjamin Cummings

The metabolic processes and the normal regulation of blood glucose levels are depicted in Figure 2.

B. Disease Physiopathology

Type 1 DM is characterised by the loss of β-cells. It is mainly caused by an autoimmune process, where T-cells of the immune systems attack and destroy β-cells, thus leading to insulin deficiency. The insulin-dependent uptake of glucose in cells is no more possible, and the main consequences are a high level of blood glucose and low level of fuel for body cells. Typical diabetes complications include cardiovascular disease, stroke, chronic kidney failure, foot ulcers, and damage to the eyes. However, *prevention* and *treatment* are possible: Type 1 DM must be firstly managed with insulin injections; however, medical evidence shows that patients affected by Type 1 DM benefit from a healthy diet, sport activity, maintaining a normal body weight, strict controlling glycaemia, and avoiding use of tobacco. For this reason, Type 1 DM is subjected to several initiatives for supporting the self-management of the disease.

V. Type 1 DM self-management

Diabetes is nowadays one of the most common and known chronic disease. Data from the World Health Organization (WHO) [23] refers that 1.5 million of deaths are attributed to diabetes each year, and that 9% of the adults population is affected by diabetes. For this reason, the self-management of diabetes is nowadays supported by a wide range of systems exploiting mobile health technologies, mainly aimed at guiding patients towards healthy lifestyle changes [10], [24], [25]. The main goal is to find solutions for identifying personalised therapies and lifestyle suggestions for patients to improve their outcome.

In the following we present an ABM of Type 1 DM self-management. The whole model architecture is depicted in Figure 3: from an initial state that reproduces the health condition of a patient, a low level simulation of the metabolic system (described in the following) is performed. From the simulation results, feedbacks are provided to the patient, who could then modify his/her behaviour accordingly, if needed.

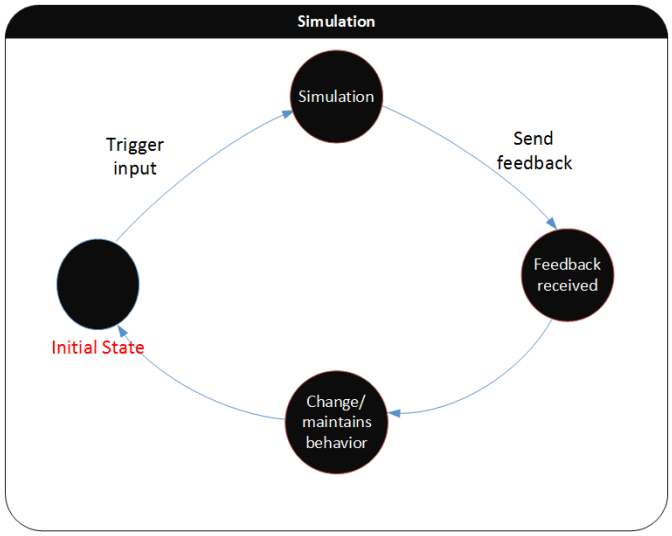


Figure 3. Simulation Architecture

A. Type 1 DM Model

We model the metabolic system as a set of interacting agents, where each agent is a set of cells conducting the same activities. In particular we include the main organs (or set of cells) involved in metabolic processes—as shown in Figure 1. Agents then interact via an interaction medium, the environment, that models the bloodstream where agents release and retrieve molecules.

We consider the following agents:

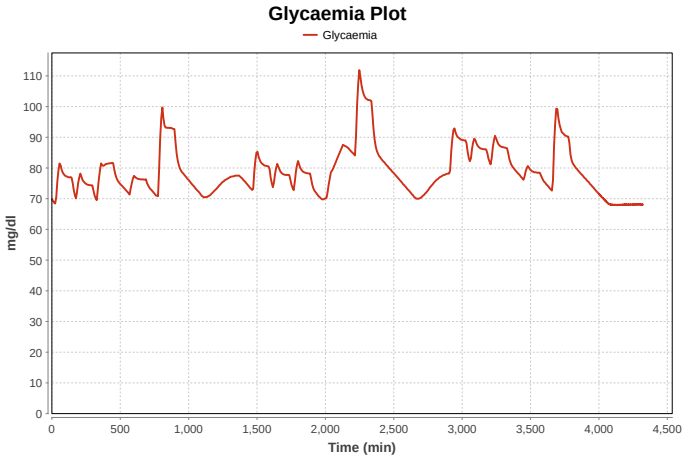
- *intestine-cells* agent — it absorbs and breaks down food substances, releasing the glucose derived by digestion in the bloodstream
- *β-cells* agent — if glucose level in the blood exceeds the threshold of 75 mg/dl it secretes insulin in the bloodstream; this process ends as soon as glycaemia get back into physiologic values
- *α-cells* agent — if glucose level in the blood falls below the threshold of 70 mg/dl it secretes glucagon in the bloodstream; this process ends as soon as glycaemia get back into physiologic values
- *liver-cells* agent — if glucagon is available in the blood, it begins the process of glycogenolysis, breaking down glycogen molecules and realising glucose in the blood; plus, if glucose level in the blood exceeds the threshold of 75 mg/dl, it uptakes glucose from the blood and begins the process of glycogen synthesis
- *muscle-cells* agent — if insulin is available free in the bloodstream, it absorbs glucose and begins the process of glycogen synthesis; plus, during physical exercises, it consumes – according to the type of activity – a balanced quantity of glycogen
- *brain-cells* agent — it continuously absorbs glucose from the blood

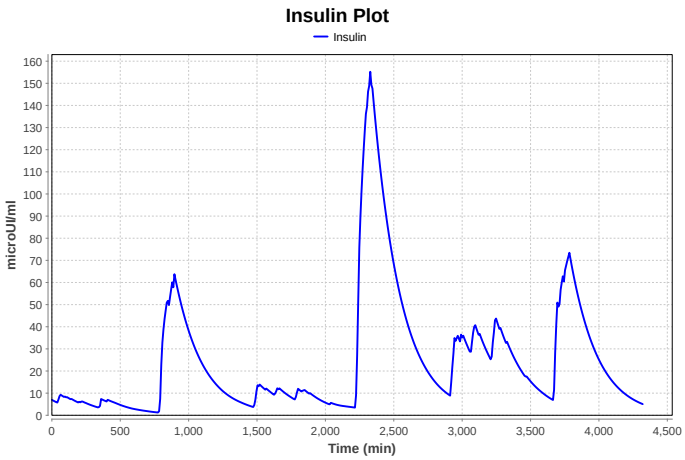
The model of Type 1 DM is hence obtained by simply stopping the β-cells agent.

B. Early Simulation Results

The model is implemented on top of the MASON infrastructure [26]. We here presents the results obtained with the low-level model, showing that it correctly reproduces the dynamic of the metabolic system in both the cases of healthy and Type 1 DM patient. We leave to future work the implementation and verification of the whole self-management system.

Figure 4 shows the dynamic over 3 days of glucose, insulin, and glucagon concentration in blood in a healthy patient. There, the glycaemia value varies during the day following meals (breakfast, morning snack, lunch, afternoon snack, and dinner). Insulin and glucagon follow these dynamics: *(1)* insulin increases as a response of glucose increase, while *(2)* glucagon is secreted mainly during the night when patient does not eat.





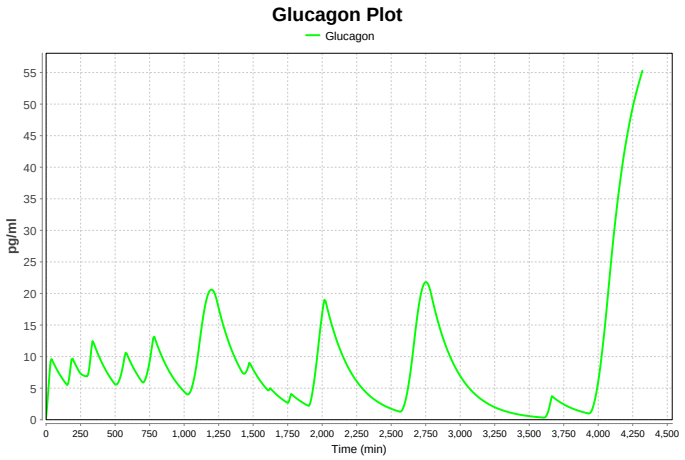
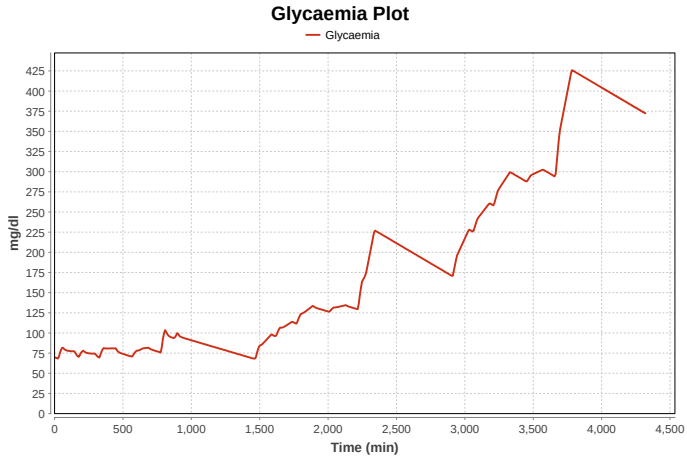
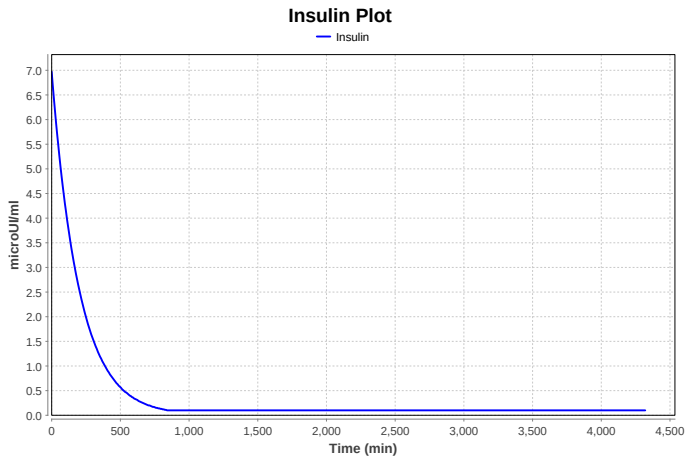


Figure 4. Simulation results for a healthy patient





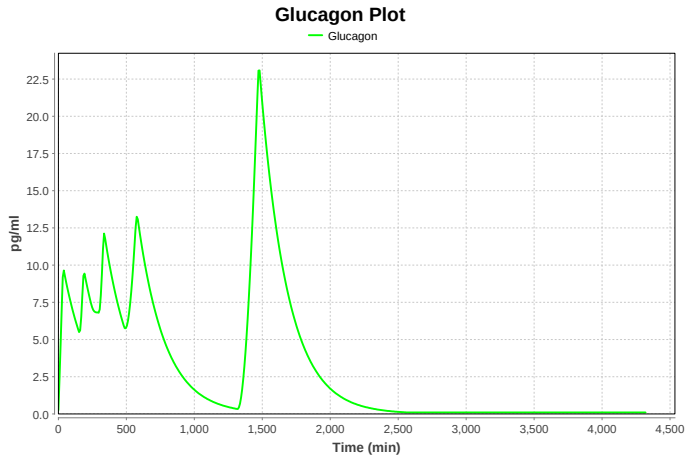


Figure 5. Simulation results for a patient with Type 1 DM

Figure 5 shows the dynamic over 3 days of glucose, insulin, and glucagon concentration in blood in a Type 1 DM affected patient. There, the glycaemia value is no longer under control, and the patient enters soon into a hyperglycaemia state. Insulin is no longer produced, and glucagon also is no longer secreted, since glucose concentration is over the threshold.

We plan to interpret these dynamics as predictions on the state of the patient in the close future, and to use this information as input for algorithms – such as artificial neural network and rule-based systems – that autonomously identifies suggestions on the best behaviour that the patient should follow in order to contain the Type 1 DM effects.

VI. Conclusion

In this position paper we explored some future directions in the field of self-management of chronic diseases. Given the widespread diffusion of chronic diseases, a set of specific interventions are suggested by the health organisations, such

as PAHO and WHO. Among the others, self-management is identified as a promising approach to decrease health spending in chronic diseases and to improve the patients quality of life. IoMT seems to be crucial for implementing the idea constituting the self-management approach in the real world.

In particular here we propose the adoption of ABMS as a built-in tool – within a IoMT infrastructure – that can automatically characterise health state of patients, providing them with feedbacks for their daily life. As our case study, we focus on a specific disease, the Type 1 Diabetes Mellitus, building our first model of chronic disease self-management, thus also showing the general feasibility of our approach. Finally we provide some preliminary simulation results illustrating the behaviour of our model of the metabolic system both in a healthy individual and in a Type 1 DM patient.

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