A global methodology for modeling and simulating medical systems

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***Abstract*—A mathematical representation of patient or device is presented by a number of variables which are defined to represent the inputs, outputs and a set of equations describing the interaction of these variables. This paper proposes a global methodology for modeling and simulation medical systems and human body, in order to analyze the performance and the quality of services of all system components. Beginning by defining a new prototype of a global and flexible architecture of mathematical model of human body, that is able to contain required data. Then, describing the simulations representation, by mentions in details the core simulator components, analyzer, and the quality of services indicators. Simulation of mathematical models provides useful tools for diagnosis and analyzing the interactions between efficacy, therapies, side-effects, and outcomes. This will help to better understand the human organism control, to analyze experimental data, to identify and quantify relevant biophysical parameters and to design clinical trials.**

Keywords—modeling, simulation, medical systems, quality of services, architecture, mathematical model, diagnosis, control, clinical cases.

I. INTRODUCTION

The definition of medical devices is wide and includes instruments, devices, equipment, materials, and products. The world health organization defines medical devices as "any instrument, apparatus, implement, machine, appliance, implant, in vitro reagent or calibrator, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purposes of: diagnosis, prevention, monitoring, treatment or alleviation of disease; investigation, replacement, modification, or support of the anatomy or of a physiological process; control of conception" [1].

Previously, without simulation, there was a delay in work progress and the cost was more expensive. There was a need for providing higher work productivity, minimum cost. Simulation modeling enables to virtually investigate many prototypes and analyze all inputs and outputs, constraints and device behaviors. Simulation was defined as a technique or a method, used in health care education fields [2] and assessment, to replace real patient with scenarios designed to promote knowledge and experiences.

Advances in information technologies and systems, reflect an increasing in medical devices domain, which guide to better diagnosis and delivery of treatment, enhancement in usability and new functionalities. The importance of simulation modeling in medical instrumentation is arriving to reduce medical errors, solve health problem and to improve patient safety. Recent models in the literature suggest that simulation modeling techniques are useful tools for analyzing complex systems in critical care [3]. These simulation techniques are usefulness in understanding real problems in critical care [4, 5].

The study of the structure of the human body and its parts is called anatomy while physiology is the study function of those parts [6]. These two complementary scientific disciplines, affect the fundamentals that allow us to understand the human body. The study of the function and structure are inseparable. Indeed, the function always reflects structure. That is to say that an organ can only perform the functions permitted by its structure. For example, the heart can pump blood only in one direction because of the structure and arrangement of the heart valves [7].

Each organ has a specialized functional structure that performs an essential activity that no other body can perform in his place. These construct level of systems; each system consists of organs that work together to perform a single function. All systems cannot work completely independently; they all work as one organism (ex. digestive, cardiovascular, muscular and respiratory systems). Noting that, all systems work together to maintain human life, by maintaining controlled factor or what can we called physiological variables. These variables must be maintained by the system that analyzes the data it receives and determines the appropriate response.

We can resume the variation of these variables as follow: an external event affect a physiological variable, a receptor sensor detect this modification, and send an input signal about this detection to the system to control it. The control system send an output signal to the effectors' actuator, the signal send by the actuator acts on the intensity of the stimulus feedback. Simulation this procedure helps to better understand the whole system.

Biomedical simulation [8, 9, 10] test is a new type of medical test, a kind of simulation medical procedure performed to detect, diagnose, analyze, or monitor biomedical equipments [11, 12]. The test is used to assess scientific aptitude of biomedical equipments. The performance of simulation must be evaluated to determine whether it is optimized or not. Hence, in measuring the quantitative performance of it, mean error is implied which was to determine the error between the targets and the output.

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Innovations in biomedical technologies are seen as being able to provide solutions to improve the quality and the efficiency of healthcare systems [13]. There is a need to improve the quality of the services (QoS) provided, by ensuring biomedical are fit for purpose, which give an opportunity to develop new services or new diagnosis with an objective of upgrading and improvement. In other words, a set of quality of services must be satisfied.

This work provides a new comprehensive toolset to tackle the issues of system modeling, analysis, QoS system integration and verification.

The aim of this research is to design and develop a global methodology for modeling and simulation human body and biomedical systems. The outline of this paper is as follows: section II presents architecture of the model, mathematical model of human body, simulations structure and simulator representation. Section III gives the QoS indicators, schema and evaluation. Section IV is dedicated for conclusions and perspectives.

II. ARCHITECTURE OF THE MODEL

A. Introduction

Humans must keep their limits, move, react to changes in their environment, ingest and digest food, have a metabolic activity, eliminate waste, reproduce and grow. The distribution of vital functions, between different systems, leads to interdependence of all body cells [14, 15]. The picture below (figure 1) shows the interdependence of body systems, where the integumentary system protects the whole body against the environment. The digestive system and respiratory system interact with the environment and provide respectively nutrients and oxygen to the blood which then distributes to all cells. Metabolic wastes are eliminated from the body through the urinary system and the respiratory system.

None of the systems are working completely independently, they all work well-being of the whole organism. For example, the digestive system and the respiratory system interact with the environment and provide respectively nutrients and oxygen to the blood which distributes them to all cells.

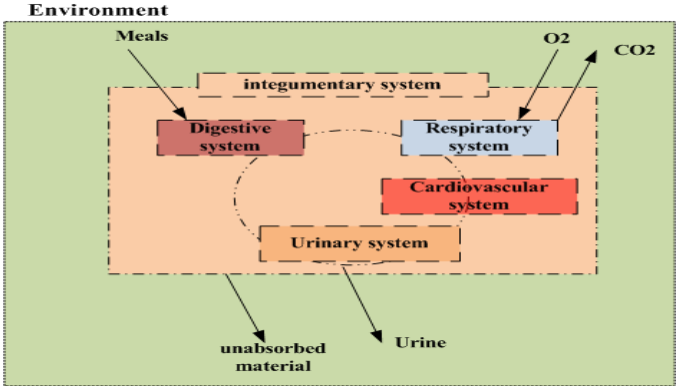

Fig. 1. interdependence of body systems

In human body there are a lot of physiological variables that must be maintained or controlled. Let *PV* as the abbreviation concerning physiological variable. For example: blood pressure, acidity of the blood, blood sugar level, heart rate, body temperature, and breathing rate. Any event that affects the system, reflect a change in the physiological variable, the system tends to maintain conditions that require frequent monitoring and adjustment within physiological limits.

The blood pressure is a *PV* controlled by the human body. When an event causes this *PV* to increase, pressure-sensitive nerve cells (sensors) in certain arteries send nerve impulses (input) to brain (controller). The brain interprets the messages and responds by sending fewer nerve impulses (output) to the arterioles. This causes the arterioles (actuator) to dilate (response) (figure 2).

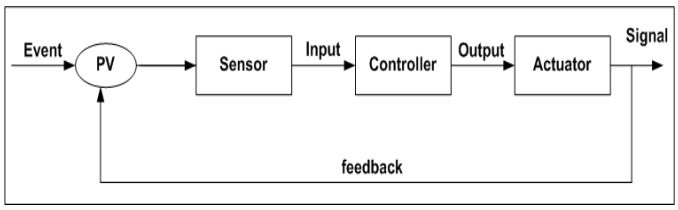

Fig. 2. physiological regulation

Figure 2 shows how human body can be interconnected to form a physiological closed-loop system.

B. Mathematical model representation

The use of ordinary, partial, and integral differential equations to model biological systems has a long history. Mathematical modeling is becoming an increasingly important subject, help to expand our ability to translate mathematical equations and formulations into concrete conclusions [16, 17]. Various distribution models have been used extensively in many fields [18].

The mathematical model of patient is a set of equations and various algorithms, where the use of parameters and constants to resituate the human body functioning.

Let *Mp* be a mathematical model for a patient, *S* is a set of system, *Pf* a set of personal information about the patient that may affect the system such as weight, stress, etc…, *Dm* a set of daily meals, *Or* a set of body organs, *Ir* a set of internal relations for the body actors, *Er* a set of external relations between the body actors, *C* a collection of constants related to systems actors and *Par* a collection of parameters. *PV* is a collection of physiological variables reflecting the state of a patient. Both *C* and *PV* are numerical values that may be used by the relations (equations) in the model.

Let *W* is the weight, *St* is the symbol to indicate stress, *Sp* to indicate if the person do sport, etc...

$$Pf = \{W, St, Sp \ldots\} \quad (1)$$

Let *B* is the set of breakfast food values such as calories fat protein etc.., *L* the set of lunch food value, *D* the set of dinner food values and *Af* the set of additional portions values such as snacks.

$$Dm = \{B, L, D, Af\} \quad (2)$$

Let Or_i is an organ in human body

$$Or = \{Or_1, Or_2, Or_3 \ldots Or_n\} \quad (3)$$

Let Ir_i are an internal relation (mathematical function) for an Or_i that uses values from $SC \in Or_i$ and $SPar \in Or_i$.

$$Ir = \{Ir_1, Ir_2, Ir_3 \ldots Ir_n\} \quad (4)$$

Let Er_i are an external relation (mathematical function) between two or more Or_i that uses values from C and Par.

$$Er = \{Er_1, Er_2, Er_3 \ldots Er_n\} \quad (5)$$

Let $SName$ is the name of the body system (such as Digestive system), SC is a set of constants related the concerned S_i and SPV is a set of physiological variables related to concerned S_i. SC is a subset of C and SPV a subset of PV. Noting that, intersections between SPV of different systems are not necessarily empty, because some physiological variables may affect several systems so they are common variables between these systems.

$$S = \{S_1, S_2, S_3 \ldots S_n\} /$$

$$S_i(Sname, SC, SPV, Ir, Er) = \cup_{j=1}^{n_i} Or_{ij} \quad (6)$$

Let Par_i are input parameters for the system, $Par = U_{Spar}$, $SPar \in S_i$

$$Par = \{Par_1, Par_2, Par_3 \ldots, Par_n\} \quad (7)$$

Let C_i are predefined constants for the system / $C = U_{SC}$, $SC \in S_i$

$$C = \{C_1, C_2, C_3 \ldots, C_n\} \quad (8)$$

Let PV_i are physiological variables controlled by the system / $PV = U_{SPV}$, $SPV \in S_i$

$$PV = \{PV_1, PV_2, PV_3 \ldots, PV_n\} \quad (9)$$

Finally $Mp = (Pf, Dm, S)$ would be a global and flexible model applicable to any analyzer for a patient and may integrate one or many body systems constituting a case of study or even all body systems.

C. Simulation structure

This part is described as "Core simulator components", shown in figure 3, contains two simulations sections related with each other's by input/output hardware interface components.

The first section described as "Patient simulation" (PS) simulate the patient using a mathematical model; the patient model has been simulated to better understand the mechanisms of the human organic system. There are many constants and parameters involved in the model. There are usually decided upon collecting data or experimenting. These models are the best way to simulate patient physiology and pharmacology and provide responses in real time to whatever treatment has been given.

The second section named as "Device Simulation" (DS) used to describe the simulation of medical devices using mathematical model equations, with the ability to simulate also sensor, actuator and controller. This mathematical model is used to mimic the function of medical device by simulating hardware and application, which help to form a complete system simulation.

The idea from simulation is to improve the design and testing of medical devices, which can be simple devices to be used in educational fields or complex devices that combine mechanical models with computer stations.

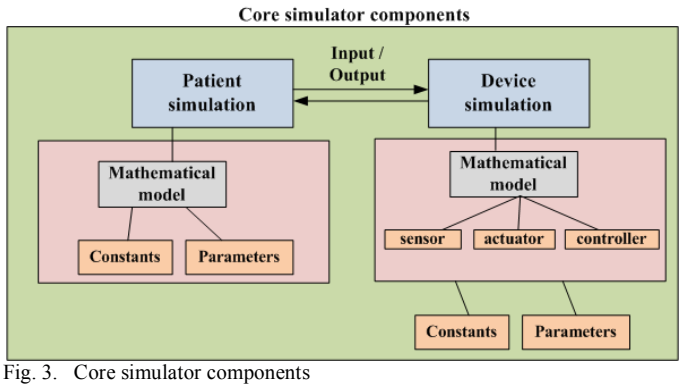

Fig. 3. Core simulator components

The mathematical models have been successfully developed for testing, simulation optimization, control, design and diagnostic. The core simulator components can represented as a tuple <*Mp*, *Md*, *S*, *A*, *Cr*> where *Md* the mathematical model of device, *S* for sensors, *A* for actuators, and *Cr* for controller

We can simulate the biomedical equipments, by simulation patient level, sensors and actuators levels, and simulating the electronic hardware. We have previously successfully implementing and simulating a mathematical model of the human body [19], using Keil [20] development tools designed for ARM processors. Sensors and actuators were also simulated using codes that simulate their functions.

Keil is used as software development tools for embedded microcontroller applications. It has a simulator part that simulates most features of a microcontroller without the need for target hardware. By using it, we can test, debug and simulates codes and a wide variety of peripherals. The advantage of using Keil in our work is to define a model that works with embedded *C* language and can be implemented in a microcontroller.

D. Simulator representation

Medical definition of simulator is "a device that enables the operator to reproduce or represent under test conditions phenomena likely to occur in actual performance" [21]. Lack of communication and lapses human error are the most potential accidents in medicine, which leads medical simulation as a powerful technique to bridge this gap.

When talking about simulator we talk also about scenarios, patient and devices (figure 4). The body of the simulator is composed from a scenario, patient and device. In

case of patient, the simulator use more sophisticated technique using mathematical model differential equations of a patient's physiology, with specific constants and some parameters versus time for example meals. Also in case of device, the simulator use also advanced model and constants and parameters versus time if needed.

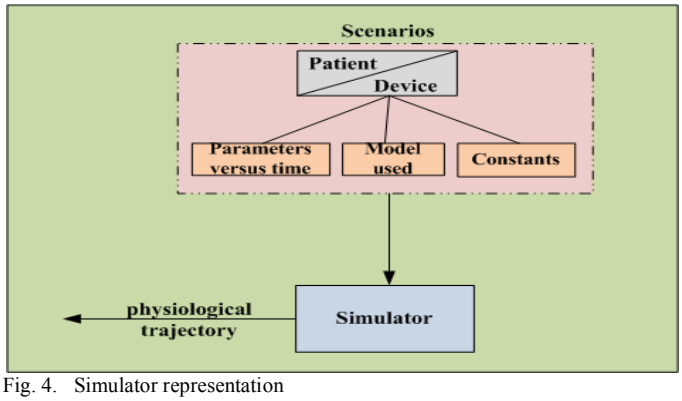

Fig. 4. Simulator representation

We can for example simulate misuse of a particular device, by changing initial configuration or by creating a problem, in utilization, will give a corruption in result. In other situation, the use of practical medical scenarios helps to illustrate effective equipment and diagnosis procedures.

The simulation help to optimize the performance of devices avoid risks on patients and an evolution the treatment of disease. Taking many mission-critical simulations by creating many population scenarios, help minimize deficiency of accuracy and having a good performance and quality of service.

One of the most important uses of simulation output analysis regards the comparison of competing systems or alternative system configurations [22]. An important feature of simulation is its ability to allow the experimenter to analyze and compare scenarios quickly and efficiently.

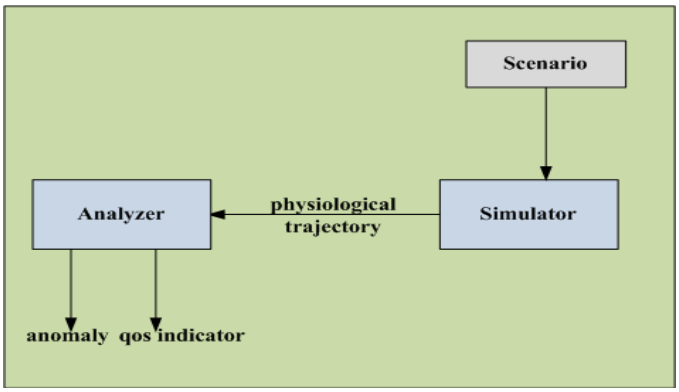

Fig. 5. Analyzer representation

Figure 5 describes that using simulator and then from a scenario we can generates the physiological trajectory. Analyzing this trajectory help to know if there is anomaly or not, and to generate values concerning the indicator of the quality of service. The objective is to provide the expected services in a dependable way, and maintaining the required Quality of Service levels. In other words, a set of Quality of Services must be satisfied.

III. QoS INDICATORS

Quality of Service (QoS) in the context of service oriented architectures (SOA) has received considerable scientific attention. While existing work on QoS has focused mainly on availability, reliability, security and cost, QoS issues related to data access and retrieval are rather less investigated. Maintaining QoS is equal to maintain the *PV* in a normal state.

Each *PV* controlled have a maximum and minimum levels that these values must reach without arriving to the dangerous state. Estimates calculation of the range of controlled values depends on the *PV*, controlled and the some characteristic of human body. However, this is only estimation; individual values vary considerably from this average value. Noting that, a normal value is the reliable value that remains constant from day to day and changes only slightly from year to year.

We are alive because important *PV* in our body are regulated automatically and so remain within certain levels. We can imagine what may happen without these controls by thinking about the consequences of a control failure. The human body has his main automatic control mechanisms. Feedback is a key concept. The actual values of *PV* are sensed, fed back and used to control the system. The behavior of these controlled variables is typically described by differential or difference equations in the time domain.

When change in a state of a *PV* is occurred upon an event, negative feedback responses are triggered to bring the *PV* back to its normal point. The sensor, controller and the actuator play a role as a parts of negative feedback response

The control specifications of the *PV* may refer to a static value or to a dynamic value that change by time. The study of each system helps to identify these variables, which need to be manipulated and by how much, in order to achieve given desired specifications.

Consider α_i range of value that *PV* can reach from normal value to the maximum / α_1 is the highest value,
Consider β_i range of value that *PV* can reach from normal value to the minimum / β_1 is the lower value.

$$\{\beta_1, \beta_2, \beta_3 \ldots, \beta_n\} < PV < \{\alpha_n, \ldots. \alpha_3, \alpha_2, \alpha_1\} \qquad (10)$$

A. QoS schema

For each scenario a quality service is recovered. After creating and simulating millions of scenarios, we can use the information of each scenario to retrieve a more comprehensive quality of service that will not depend on the scenarios.

In fact we don't generate scenarios (figure 6), but we create a system that allows generating multiple scenarios to retrieve more relevant information. We can modify the number of device and their characteristics (N_d), the number of patients and their characteristics (N_p), or a mix of patients, devices and parameters ($N_{s,p,d}$) of different scenarios. Creating multiple scenarios, in order to simulate and analyze data of results. To create them, we need many population and prevalence data, and with a number of generic pathways physiological trajectory to arrive to calculate the proper

quality of service.

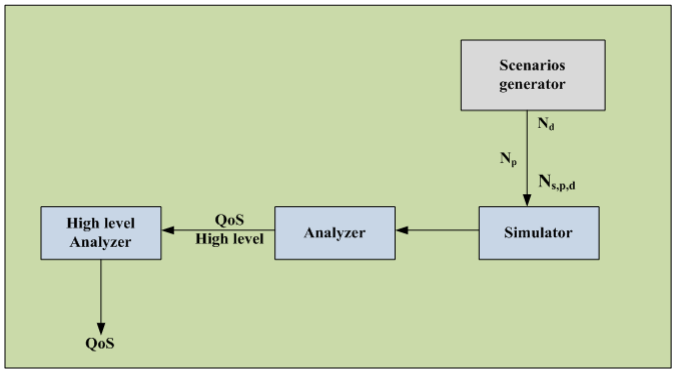

Fig. 6. QoS indicator schema

Create virtual population of many cases accompanied by sets of n parameter representing n virtual cases (figure 7). A population is considered as an array of cases. Each case has characteristics represented by fixed and variables parameters.

A virtual subject with type 1 diabetes is represented by a model of glucose regulation and its parameters. The simulation environment includes 10 synthetic subjects defined by 10 parameter sets (see Figure 7).

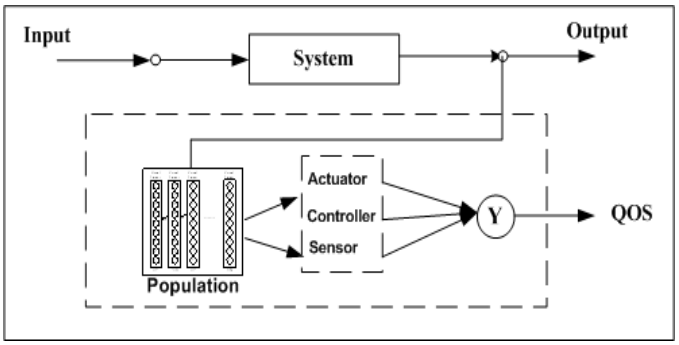

Fig. 7. QoS input and output

In figure 8, the patient generation is modeled as non-FIFO, and considered as work-conserving system because of the presence of (*t, Par*, *C*) and feedback. Noting that, Non-FIFO method is used in many domain fields [23, 24].

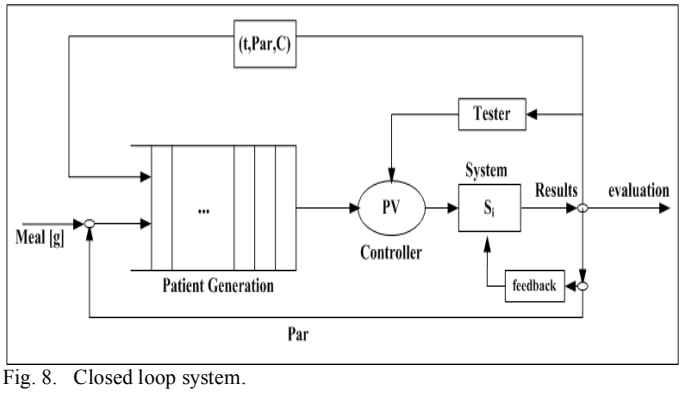

Fig. 8. Closed loop system.

In a system there is a *PV* to be controlled and tester that are interconnected to form a physiological closed-loop system. A high-level overview of the system allows creating many clinical cases that can benefit from closed-loop systems.

B. *QoS evaluation*

We use two techniques that help evaluate the calculated QoS value. The first one calculates an index of severity IG_H (g) which indicates the severity of the case studied. It can be computed by approximating the integral of f (t) where f (t) is the function representing the state of the medical devices on a time interval $[t_i\ t_f]$. The indicator has an objective; it compares the diabetic systems with the normal system.

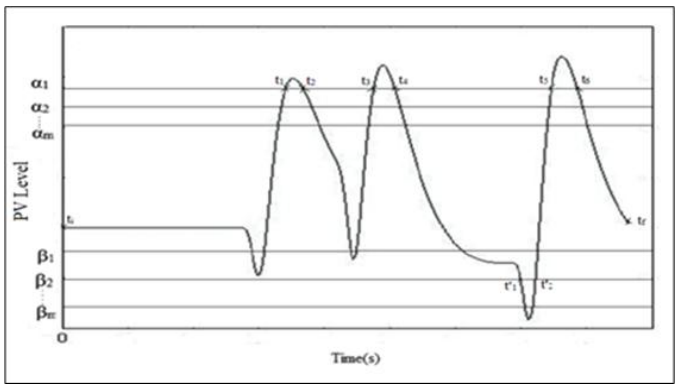

Fig. 9. Index of severity representation

The graph above (figure 9) describes the simple indicator in an arbitrary case that we try to propose and apply it in the QoS tester in order to help us to evaluate it. This IG_H can be computed by approximating the integral of f (t) using Matlab built-in function [19].

The second one, by using a consensus error grid [25, 26, 27, 28], that helps to estimate the error of the performance of devices. The grid is a simple representation in order to estimate the error of the performance of sensors, actuators and controllers. The performance of the algorithm was analyzed with the consensus error grid using data sets generated by virtual patients and parameters changes [29] (figure 10).

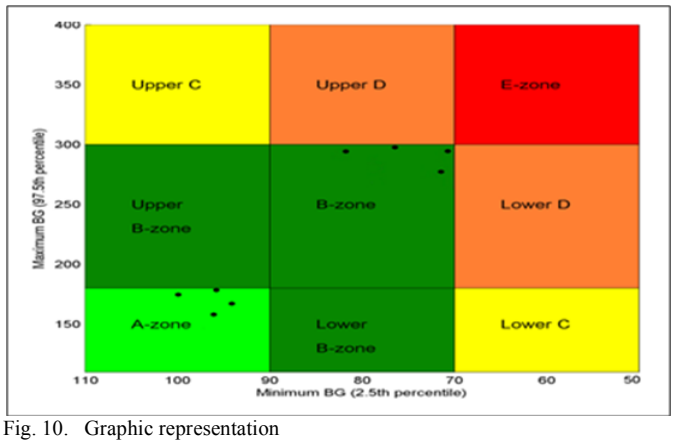

Fig. 10. Graphic representation

IV. CONCLUSION

We have provided a global flexible architecture of human body model with mathematical representation. A full simulation representation of the simulator components, analyzer part and the QoS indicator schema and the evaluation method used. The purpose of this architecture is to have a complete environment with the ability to simulate medical equipments, and test their performance.

Further, future work will be carried out to improve the assessment correctness of the estimation techniques.

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