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Artificial Intelligence in Medicine 27 (2003) 305–334

Artificial Intelligence in Medicine

www.elsevier.com/locate/artmed

Anthropic agency: a multiagent system for physiological processes

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Received 26 August 2002; received in revised form 18 October 2002; accepted 18 October 2002

Abstract

Multiagent systems are powerful and flexible tools for modelling and regulating complex phenomena. In fact, a way to manage the complexity of a phenomenon is to decompose it in such a way that each agent embeds the control model for a portion of the phenomenon. In this perspective, the cooperative interaction among the agents results in the controller for the whole phenomenon. Since the portions in which the phenomenon is decomposed may overlap, the actions the single agents undertake to regulate these portions may conflict; hence a balanced negotiation is required. A class of complex phenomena that present several difficulties in their satisfactory modelling and controlling is the class of physiological processes. The purpose of this paper is to introduce a general multiagent architecture, called *anthropic agency*, for the modelling and the regulation of complex physiological phenomena.

Keywords: Physiological process control; Anthropic agency; Negotiation; Glucose–insulin metabolism processes

1. Introduction

Multiagent systems [35] are collections of interacting heterogeneous entities, called agents. An agent can be defined as a special kind of physical (computer or robot) or logical (software) entity that presents the properties of autonomy, social ability, reactivity, and proactiveness [37]. A multiagent system is a recognised powerful and flexible tool for modelling and controlling some complex phenomena, since it can host, within its component agents, the coexistence of multiple partial models of a given phenomenon

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0933-3657/03/$ – see front matter
doi:10.1016/S0933-3657(03)00008-3

[3,16]. In fact, the complexity of a phenomenon can be usually decomposed in such a way that each agent embeds the control model for a portion of the phenomenon [22,23]. Hence, each agent controls only some aspects of a phenomenon and a complete controller for the whole phenomenon emerges from the cooperation process among agents. The actions the agents undertake to control their portions of the phenomenon may conflict, as a result of the ''overlapping'' of the controlled portions. This conflict can be tackled with the identification of an appropriate negotiation paradigm [24] to be employed in the multiagent system. An important class of complex phenomena that present several difficulties in their satisfactory modelling and controlling is the class of physiological processes [20]. Quite seldom a physiological process can be modelled by a complete description that is useful to design an adequate controller.

The purpose of this paper is to introduce a general multiagent architecture, called *anthropic agency*, for the modelling and the regulation of complex physiological phenomena. We illustrate the general structure and the properties of the architecture with particular emphasis on the paradigm the agents of anthropic agency adopt to negotiate a global result from their, possibly conflicting, partial views. We also describe an implementation of this architecture to regulate the glucose–insulin metabolism processes in diabetic patients.

The anthropic agency architecture is based on three groups of agents that perform three basic activities: knowledge extraction, decision making, and plan generation. All these agents are software entities that have the classical software properties: upgradeability, scalability, and reusability. Within anthropic agency we embedded a negotiation mechanism that exploits a mediator to fuse together the decisions (about the controlling actions to be performed) proposed by the agents, which are based only on their partial views of the phenomenon to be controlled. In this way, a single decision that maximises the social welfare of the whole system is determined.

The validity of the proposed paradigm has been experimentally verified by simulating the metabolism of a diabetic patient and by employing an implementation of the anthropic agency to regulate the insulin and glucose levels of the patient.

The main original contributions of this paper are the following.

- We propose a novel approach, based on multiagent systems, to address in a demonstrated effective way the regulation of physiological processes. In fact, to the best of our knowledge no other multiagent-based biomedical control system has been developed and demonstrated to work so far.
- We concentrate in particular on the important problem of regulating the glucose–insulin metabolism processes in diabetic type I patients. The continuous time regulation activity provided by our anthropic agency solution to this problem significantly differs from the traditional solutions based on the (sometimes computer-assisted) preparation and injection of insulin doses few times a day.
- We introduce an interaction paradigm for the negotiation of a common decision among agents with the adoption of a mediator.

The final goal we envisage for anthropic agency architecture is the control of *real* physiological processes. However, up to now it is not conceivable to have a multiagent system controlling these processes on a real person, mainly due to security reasons and to the lack of an adequate technology for building the agents. We believe that the

next-generation agent technologies, based on the advent of the nanotechnologies, will provide for the possibility of embedding the anthropic agency systems in the human body. Given these considerations, the current major application of anthropic agency is in the investigation, by simulation, of the interdependencies among controllers and physiological processes. By means of anthropic agency, it is possible to analyse the connections between known models of a phenomenon and newly devised control models, for instance, between the known models about pancreas and the model of the effects of a new drug. Moreover, the anthropic agency can be also proficiently exploited to monitor physiological values, to diagnose pathological states, to detect body-implanted hardware and software malfunctions, and to acquire, process, and communicate data between patients and physicians. However, these last possibilities have been not yet fully explored in our experimental activity.

This paper is organised as follows. In Section 2, we overview the reasons at the basis of the need for distribution in the field of control systems for physiological processes and we review the state of the art of multiagent-based control systems. In this way, we are able to insert the contributions of our work in a general coherent framework. In Section 3, we introduce the structure and the underlying philosophy of the anthropic agency general architecture. In Section 4, we describe in detail our implementation of the anthropic agency architecture in the practical case of the regulation of the glucose–insulin metabolism processes. Section 5 shows the experimental results we obtained from the tests performed on the implemented anthropic agency. In Section 6, we summarise the main advantages of our approach by critically evaluating the experimental results. Finally, Section 7 concludes the paper.

2. Distribution in biomedical control systems

2.1. General principles of control distribution

In the context of processes control, an alternative to the classical approach based on a single monolithic controller is the *decentralisation* based on the *divide-et-impera* principle that conceives a phenomenon as composed of a set of (related) sub-phenomena [1,13]. While in the first case the model of the whole phenomenon to be regulated is embedded in the unique controller unit, in the second case a number of partial models of the phenomenon are embedded in the decentralised controller units. This is to say that each one of these controller units can regulate just a single part of the entire phenomenon, as a traditional control system does. We can also say that a controller unit is the sub-controller of a sub-phenomenon of the entire phenomenon. A control system for the global phenomenon simply emerges from the structured interaction of the partial controller units.

The above abstract idea of decentralisation, which applies both to phenomena that are distributed by their nature and to phenomena that are considered as distributed for convenience, can be expressed more formally. Let us represent the global model of a phenomenon as a function f with domain the space $\Re^n$, whose dimensions constitute the input variables of the model, and with codomain $\Re^m$, whose dimensions describe the output variables that characterise the behaviour of the phenomenon modelled by $f : \Re^n \rightarrow \Re^m$.

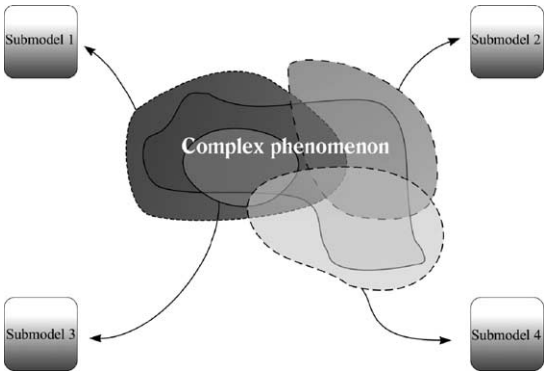

Fig. 1. An example of the decomposition of a complex phenomenon in a set of sub-phenomena represented by sub-models.

In general, given a phenomenon, there are many different ways to decompose it. The ways in which the whole phenomenon may be decomposed in sub-phenomena have not definitely assessed rules yet. The identified sub-phenomena may enjoy different relations [3]. For example, the schema of Fig. 1 presents a phenomenon decomposed in four sub-phenomena that partially or completely overlap, namely, that are subject to containing relations. As a result, the models $\{f_w\}$ of the sub-phenomena (f_w being the model of the sub-phenomenon w, with $f_w : \Re^{n_w} \rightarrow \Re^{m_w}$, where $\Re^{n_w} \subseteq \Re^n$ and $\Re^{m_w} \subseteq \Re^m$) are related to each other, namely, their domains and they codomains intersect. In general, there are no a priori imposed constraints on the $\{f_w\}$.

The advantages of the decentralisation of control lie mainly in the possibility to devise models with higher degree of approximation with respect to the real phenomenon, because the decomposition of phenomena allows to develop sub-models for very specific contexts. Moreover, a complex global model usually depends on several parameters that are difficult to identify and to measure. Another advantage is connected to the possibility to employ alternative sub-models for describing the same phenomenon, as in the multimodel approach of [25]. As a consequence, the decentralisation is particularly useful for domains in which it is rarely the case when phenomena are satisfactory captured in assessed models, like human physiology [20,36]. In this paper, we illustrate a decentralised control system for glucose–insulin metabolism in which partially overlapping models of glucose level regulation coexist.

The decentralisation of controllers is not the only role that distribution plays in control. Another (orthogonal) role is connected to the *functional distribution* of the control activities that can be applied to the design of controllers. The controller can be itself a distributed entity. In this paper, we adopt a distribution of functions in a controller that is inspired to the classical robotic approach [19]. As shown in Fig. 2, we consider a controller structured in three main steps: knowledge extraction, decision making, and plan generation.

The knowledge extraction step extracts high-level information from low-level data received from sensors. The parameters it produces describe the state of the controlled phenomenon. A decision involves a proposed new state and its importance (with respect

Fig. 2. Distribution of the functions of a controller in three main steps according to the robotic approach.

to the control task). The decision making step generates a set of decisions and does not consider the feasibility of the actions needed to reach the states involved by the decisions. The plan generation step knows the description of the actions the actuators can actually perform and decides the ones to be undertaken and the order in which they have to be carried out. Sometimes, the plan generation step requires the execution of a new decision making step in a circular fashion. To summarise, the activity of a controller can be thought as performed in three steps: the first one related to the perception of the current state of the phenomenon to be regulated (knowledge extraction), the second one related to the generation of the desirable new states (decision making), and the third one related to the actions that are actually performed to reach these states (plan generation).

Given the two dimensions of distribution, the way in which the controllers and their components are implemented is still an open issue. In this paper, we illustrate a general physiological processes control system, the anthropic agency, whose implementation is based on the modern paradigm of distributed artificial intelligence called *multiagent systems* [16,35]. We remark that, in our approach, we adopt both the two kinds of distribution illustrated in this section. The agents are the elementary units resulting from the decentralisation of control and from the distribution of control activities. The interaction among agents enables the multiagent system to effectively control the whole phenomenon.

2.2. Multiagent-based control systems

In literature there are some other examples, most of them oriented toward manufacturing, of distributed control systems based on the multiagent paradigm. In this section, we review the most significant of these systems.

Norrie and Shen [28] survey some projects related to the multiagent systems approach for developing distributed intelligent manufacturing systems. They conclude that the relevant issues in multiagent-based manufacturing control systems are: agent technologies for enterprise integration and supply chain management, agent encapsulation, system architectures, dynamic system reconfiguration, learning, design and manufacturability assessments, distributed dynamic scheduling, integration of planning and scheduling, concurrent scheduling and execution, and factory control structures.

Balduzzi and Brugali [6] propose a novel approach to the control of manufacturing systems via agents interaction. Their main contribution consists in the introduction of two kinds of agents and in the definition of the collaboration paradigm for such agents. The first kind of agent is the production agent that manages stores and machines and enforces capacity and temporal precedence constraints on them. The second kind of agent is the control agent that manages the flows of parts among production agents in order to

guarantee the desired production target and the balance of the machine loads. The arrangement of the agents is locally hierarchical in nature.

Erman et al. [15] introduce a generic control architecture suitable for single intelligent agents and for multiple cooperating agents. The generic architecture combines a task-oriented domain controller with a meta-controller that schedules activities of the domain controller. The proposed application fields for the control architecture include military defence and telecommunications.

While the previous works propose relevant architectures devoted to manufacturing and industrial applications, Hayes-Roth and Larsson [21] developed a system named Guardian composed of an autonomous agent with a flexible architecture based on a blackboard system, in which several algorithms cooperate to produce diagnosis and treatment plans under hard real-time conditions. Guardian main task is the monitoring and diagnosing of intensive-care patients. The authors specifically designed Guardian as a reference architecture for autonomous agents that monitor, diagnose, and control in real time; however, we do not know of any working implementation of such architecture for control or regulation tasks.

To the best of our knowledge there is not any biomedical control system implemented as a multiagent system. In this perspective, the anthropic agency we present in this paper is an original and significant contribution.

The major advantages of the multiagent-based control systems relate to their ability to overcome some of the drawbacks of classical control systems. For example, classical control systems for physiological phenomena are usually symmetric with respect to the variation of parameters; it makes no difference if the value of a parameter increases or decreases. This introduces an often unacceptable simplification with respect to the controlled physiological phenomena that are seldom symmetric [31]. Multiagent-based control systems can easily manage this asymmetries since their control mechanisms are coded in flexible software programs. Another advantage of the multiagent approach to control systems is the flexibility in the management of the situations that significantly differ from the standard behaviour. The main drawbacks of multiagent-based control systems are that there is no any established theoretical framework in which they and their properties (like stability and robustness to variations of the controlled phenomenon) could be investigated. This difficulty is related to the fact that the control is spread over many independent agents that interact in a sometimes unpredictable way. For example, multiagent-based control systems may have unbounded response time. In the field of physiological processes this is not a critical issue since they usually show low Shannon frequency and thus a multiagent system can perform a reasonable control action within large time boundaries. Another disadvantage is that multiagent systems are complex distributed software systems that can present difficulties in implementation and in testing [35].

3. Overview of anthropic agency architecture

Anthropic agency is a powerful paradigm to develop control systems for physiological processes shaped as multiagent systems. The name ‘agency’ derives from our conception of a multiagent system as a single machine composed of complex components: the agents

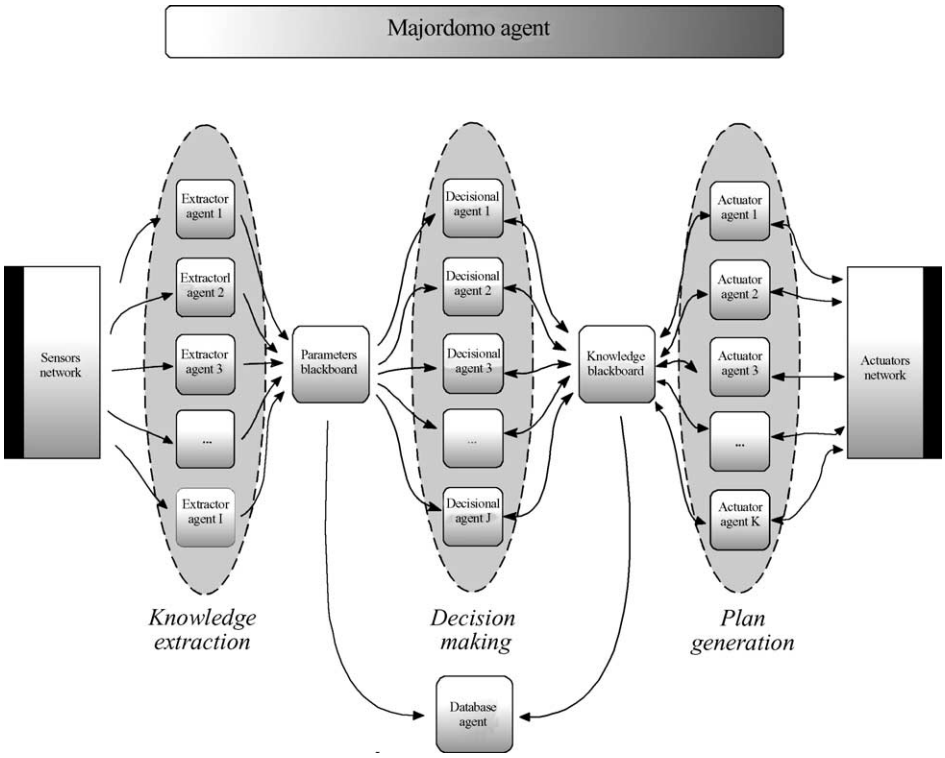

Fig. 3. The general anthropic agency architecture.

[4]. The adjective 'anthropic' (from the Greek *anthropos*, namely, man) evidences that the application field in which the agency is employed involves the physiological processes of the human being.

The anthropic agency is a multiagent control system that operates according to the three steps illustrated in Fig. 2. The architecture of anthropic agency is shown in Fig. 3. Each step is carried on by a group of agents and the interactions between these groups are mediated by shared memory areas called blackboards, which are a well-known established paradigm within distributed artificial intelligence [12,26,27] that is still investigated and improved (see, for example, [29]). The communication structure among the agents is designed to ensure decoupling and independence of agents, as a requirement for the flexibility of the whole system. To accomplish this goal, all the communications are mediated by the blackboards. More precisely:

- the agents of the knowledge extraction group communicate with the agents of the decision making group only through the parameters blackboard (the former ones write in the blackboard and the latter ones read from the blackboard);
- the agents of the decision making group communicate with the agents of the plan generation group only through the knowledge blackboard; and
- two agents belonging to the same group are not aware of the presence of each other.

The communication bottlenecks represented by blackboards do not provide a very scalable mechanism. However, we deem that, in the first stages of the anthropic agency development, the flexibility is more important than scalability. Hence, improvements to the communication mechanism could regard its scalability (e.g. by using more blackboards) and its openness (e.g. by adopting standard communication languages such as FIPA ACL [17]).

The agents performing the first control step are called *extractor agents*. An extractor agent is connected to (a part of) the sensors network from which it acquires a number of signals that it filters and processes to generate the values of a set of parameters. The signals represent the available information about the controlled phenomenon. Formally, an extractor agent i implements the extraction function $E_i(\boldsymbol{s}_i(t)) = \boldsymbol{p}_i(t)$, where $\boldsymbol{s}_i(t)$ is a vector of n_i signals from sensors and $\boldsymbol{p}_i(t)$ is a vector of m_i parameters. The parameters values generated by all the extractor agents are placed in a shared memory area called *parameters blackboard*. The parameters blackboard is managed by an agent, called parameters blackboard agent. This agent makes the blackboard an ''active'' element of the architecture. It maintains and manages the list of agents that registered to the parameters blackboard and grants them access rights.

From the parameters blackboard, the values of the parameters are read by the *decisional agents*, namely, by the agents that contribute to the second control step: decision making. Each decisional agent embeds the model of a particular physiological process aspect and it takes its decisions about what to do on the basis of its internal model, of the current values of parameters, and of the effects of the past decisions. Formally, a decisional agent j implements the decision function $D_j(\boldsymbol{p}_j(t)) = \boldsymbol{d}_j(t)$, where $\boldsymbol{p}_j(t)$ is a vector of n_j parameters read from parameters blackboard and $\boldsymbol{d}_j(t)$ is a vector of n_j decisions. A decision is a pair: a desired target value for a parameter and a weight for the value. The weight is a measure of how much the current parameter value is away from optimum and, thus, of how much the decisional agent ''wants'' to reach the proposed target value for that parameter. The models embedded by decisional agents are all different, but they may overlap in two ways: the intersection of the input parameters and the intersection of the output proposed decisions could be not null. The decisions individually taken by all the decisional agents are put in a second shared memory area called *knowledge blackboard*.

As the parameters blackboard, also the knowledge blackboard is managed by an agent that grants access to the blackboard in the same way the parameters blackboard agent does. The knowledge blackboard agent (and in particular its component called *equalizer*) acts also as a mediator between the decisional agents, which take the decisions, and the *actuator agents*, which are the executors of the decisions and that carry out the third control step in the anthropic agency. The role of equalizer in reaching a final global decision starting from partial local decisions is investigated in Section 4. Formally, an actuator agent k implements the actuation function $A_k(\boldsymbol{d}_k(t)) = \boldsymbol{a}_k(t)$, where $\boldsymbol{d}_k(t)$ is a vector of n_k negotiated decisions read from knowledge blackboard and $\boldsymbol{a}_k(t)$ is a vector of m_k actions. An action is the sequence of operations, namely, the *plan*, to produce a given parameter variation. In determining the actions to perform, the actuator agents take into account the side effects of the parameters variation (the variation of a parameter may influence the variation of another parameter) and the dynamics of already undergoing parameter variations (and of related parameters) due to previously performed actions. For the sake of simplicity, we assume that the actuator agents perform mutually exclusive actions by operating mutually

exclusive actuators, namely, the variation of a parameter of the controlled phenomenon can be performed by a single actuator agent. The actuator agents embed the models of the actions they can perform; these representations are used in the generation of the plans that accomplish the final decisions of the system.

The anthropic agency architecture is completed by two ''service'' agents, as shown in Fig. 3. One of them is called *majordomo agent* and represents the interface toward both the technical expert, who can modify the composition of the system by adding and removing agents, and the medical expert, who can inspect and tune the parameters and the functioning of the system. The other service agent, the *database agent* stores in a database the values of the parameters recorded in the parameters blackboard to allow their subsequent analysis that can be performed both automatically, by exploiting data mining techniques, and manually, by the medical expert querying the database.

In the description of the anthropic agency architecture given in this section, we have not fully addressed the role of time in its functioning. The role of time is taken into account in the next section. Here, we only outline that the activities of the agents are all asynchronous.

4. The glucose–insulin metabolism processes control anthropic agency

We have implemented the anthropic agency general architecture described in the previous section to address the regulation of the glucose–insulin metabolism processes in diabetic patients. We have chosen these physiological processes because of their significance and importance and because they have a Shannon frequency of the order of some minutes and thus they can be controlled by a multiagent-based control system that reacts in some seconds (30 s in our case). In this section, we briefly describe the diabetic pathology and the current control systems adopted in this field and then we describe in detail the glucose–insulin metabolism processes control anthropic agency we developed.

4.1. Diabetic pathology

The diabetic pathology [34] is largely widespread in the world. It has been estimated that there are 100 millions of people who suffer of this disease and that such number is increasing year by year. Diabetic patients have a double mortality rate with respect to normal people, mainly because of the presence of cardiovascular complications. There are two kinds of diabetic disease: types I and II; in this paper we focus on the type I diabetic disease. Its main effect is to reduce the sensibility to the blood glucose concentration of the pancreatic insulin production processes. As a result, the pancreas of a diabetic patient produces much less insulin than an healthy one. The effect in the glucose–insulin metabolism is that the blood glucose concentration in a diabetic patient is much higher than that of an healthy person. A long time exposition to very high values of blood glucose concentration causes serious complications to other body organs. For instance, these complications appear in the cardiovascular system, in the renal system, and in the retina. In this way, the risks of heart attacks, dialysis, and blindness by retina damage are strongly increased. Currently the main medical care consists in trying to keep the glucose concentration under control by numerous invasive insulin injections during all the day.

Each time the diabetic patient has to consider many factors to choose the current dose of insulin to inject: the amount of food he is going to eat, his current glucose concentration value, and his general physical state, just to name a few. In other words, the patient tries to make a rough approximation of his current physiological state.

Implantable infusion pumps [14,30] are currently available and some controllers have been developed [9]. However, the glucose sensor is a bottleneck in the development of a real controller since it suffers of stability problems. Once the sensor is implanted, its behaviour changes in a few days and it is not useful anymore. The target is to obtain a stable glucose sensor within the next 5 years. Meanwhile, the medical community has tried to explore other ways to improve the diabetic patients situation. These include computer-based aid systems like telemedicine and expert systems that help in insulin injection. For instance, the expert system presented in [7] can substitute the patient in choosing the correct insulin dose to manually inject. This is deeply different from our implemented anthropic agency that constantly monitors the patient and injects the correct quantity of insulin when needed.

4.2. An anthropic agency for diabetic patients

The anthropic agency for diabetic patients we developed is constituted by an extractor agent, two decisional agents, and an actuator agent. The implemented anthropic agency is not connected directly to a real patient but the human metabolism of glucose is simulated by a simulation system that allows for the introduction of some disturbs to check the performances of the multiagent-based control system. We developed this simulation system according to [11]. The anthropic agency tries to keep the glucose and insulin concentrations of a simulated diabetic patient (who cannot do it by his own) as close as possible to the concentrations of a normal person.

4.2.1. The extractor agent

The extractor agent puts in the parameters blackboard the vector $\boldsymbol{p}(t) = (I(t), G(t), \Delta G(t), A(t))$, where $I(t)$ is the current level of insulin (measured in pmol/l), $G(t)$ the current level of glucose (measured in mg/dl), $\Delta G(t)$ the current variation of the glucose (namely, $G(t) - G(t-1)$, where $t - (t-1)$ is updating time interval of the extractor agent), and $A(t)$ is the current level of the physical activity (measured in pmol/l). The extractor agent receives the values of parameters directly from the simulation system. In a real situation, the extractor agent might derive the values of parameters from the signals read from sensors (for example, from glucose and insulin sensors and from piezoelectric crystal sensor for physical activity) and from the processing of these signals (for example, the value of $\Delta G(t)$ cannot be read directly from sensors).

4.2.2. The decisional agents

The first decisional agent embeds a simplified control model of the glucose–insulin metabolism related to food adsorption involving glucose hepatic production, renal excretion, insulin utilisation, insulin production, and insulin degradation [11]. Formally, it implements a decisional function $D_1(I(t), G(t), \Delta G(t)) = \boldsymbol{d}_1(t)$ with $\boldsymbol{d}_1(t) = (\langle \bar{I}_1(t), W_{\bar{I}_1}(t)\rangle, \langle \bar{G}_1(t), W_{\bar{G}_1}(t)\rangle, \langle \Delta\bar{G}_1(t), W_{\Delta\bar{G}_1}(t)\rangle)$, where $\bar{I}_1(t)$, $\bar{G}_1(t)$, and $\Delta\bar{G}_1(t)$ are the

desired target values as proposed by the first decisional agent and $W_{\bar{I}_1}(t)$, $W_{\bar{G}_1}(t)$, and $W_{\Delta\bar{G}_1}(t)$ are the corresponding weights, according to the discussion of Section 3. This first decisional agent tries to reduce the glucose concentration during food adsorption. The second decisional agent embeds a simplified control model of the glucose–insulin metabolism related to physical activity [33], its decisional function is $D_2(I(t), G(t), A(t)) = \boldsymbol{d}_2(t)$ with $\boldsymbol{d}_2(t) = (\langle \bar{I}_2(t), W_{\bar{I}_2}(t)\rangle, \langle \bar{G}_2(t), W_{\bar{G}_2}(t)\rangle, \langle \Delta\bar{G}_2(t), W_{\Delta\bar{G}_2}(t)\rangle)$, where $\bar{I}_2(t)$, $\bar{G}_2(t)$, and $\Delta\bar{G}_2(t)$ are the desired target values as proposed by the second decisional agent and $W_{\bar{I}_2}(t)$, $W_{\bar{G}_2}(t)$, and $W_{\Delta\bar{G}_2}(t)$ are the weights of this proposal. This second decisional agent tries to keep constant the glucose level by limiting the exogenous insulin introduction when the physical activity is intense.

A decisional agent j determines whether and in what measure the current state of the physiological system (represented by the vector $\boldsymbol{p}_j(t)$) satisfies the model embedded in j. This activity is complex since the model itself can vary in time according to some of its parameters, called *pathological parameters*. For example, the glucose–insulin metabolism processes of a normal person and of a diabetic patient can be described by the same model, the two cases being distinguished by different values of some pathological parameters of the model. The physiological models are often expressed in form of sets of equations. From a set of equations it is easy to see if a state satisfy the model (in this case the state is a solution of the set of equations). However, the representation as a set of equations of a model is not very convenient to be inserted in a decisional agent, since the states that do not result explicitly as solutions of these equations are not well characterised. In fact, when the current state does not satisfy the model, the decisional agent must have a measure of how far the state is from optimum. For this reason, in decisional agents we use a matrix representation of a model. Let us describe how this representation has been obtained in the case of the first decisional agent. For given values of the pathological parameters (in this case, they are related to the insulin basal secretion level and to the glucose variation sensibility), we input in the simulation system a food absorbtion curve. The output of the simulation system are the three curves describing the behaviour over time of $I(t)$, $G(t)$, and $\Delta G(t)$. Then we changed both the input food absorbtion curve (keeping the same pathological parameters values) and the pathological parameters values (for each set of these values, varying the food absorbtion curves). The result is that, for given values of the pathological parameters, we have a set of curves describing the behaviour over time of $I(t)$, $G(t)$, and $\Delta G(t)$ with different input food absorbtion curves. We then sampled these curves at fixed instants $\bar{t}$, each time obtaining the vector $\boldsymbol{p}_1(\bar{t}) = (I(\bar{t}), G(\bar{t}), \Delta G(\bar{t}))$ that are the values of the indexes of the matrix representing the model embedded in j. The value of the element $(I(\bar{t}), G(\bar{t}), \Delta G(\bar{t}))$ is the potential value of the point, with the convention that 0 means that the point represents to the normal person's behaviour and that 100 means that the point represents the maximum pathological state. The potential value of a point is determined according to the values of the pathological parameters that characterise the set of curves from which the point has been obtained. More precisely, if $\boldsymbol{p}_\mathrm{n}$ is the pathological parameters configuration of a normal person and $\boldsymbol{p}_\mathrm{c}$ is the pathological parameters configuration of the curves from which the considered point belongs, then the potential of the point is given by

$$\alpha \prod_{i=0}^{Z} ||\boldsymbol{p}_\mathrm{n}^i - \boldsymbol{p}_\mathrm{c}^i||$$

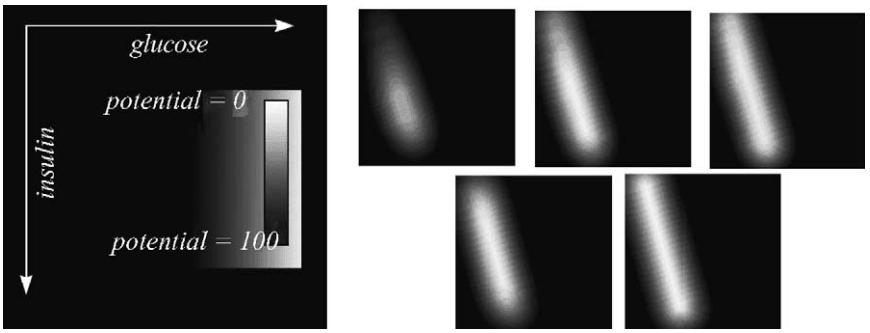

Fig. 4. The model embedded in the first decisional agent: the five images are slices of the three-dimensional matrix model corresponding to different (discretized) values of ΔG (from top left clockwise: from -0.58 to -0.56 mg/dl, from -0.40 to -0.38 mg/dl, from -0.32 to -0.30 mg/dl, from -0.04 to -0.02 mg/dl, and from 0.18 to 0.20 mg/dl.

where α is a normalisation coefficient and Z is the number of pathological parameters. The elements of the matrix whose values are not derived from this sampling are assigned values according to those of their neighbourhoods. In Fig. 4 the model embedded in the first decisional agent is shown. The ranges for the three parameters are: from 60 to 300 mg/dl for the glucose level G, from 0 to 500 pmol/l for the insulin level I, and from -0.6 to 1.2 mg/dl for the variation of glucose level ΔG.

To summarise, each decisional agent embeds a model of a physiological function; the model of a decisional agent j is represented by a (discrete approximation of a) function with n_j-dimensional domain $\boldsymbol{p}_j(t)$ and with the measure of the goodness of a specific point $\boldsymbol{p}_j(t)$ as codomain (the potential values). The less the potential value, the more desirable the point.

Different decisional agents can propose different variations for the same parameters, generating conflicts that must be tackled and solved. For example, the decisional agent D_1 may propose to decrease the glucose level after a meal and, at the same time, the decisional agent D_2 may propose to keep constant the glucose level, because the patient is undergoing an intense physical activity. Since in the anthropic agency approach we do not explicitly consider the relations among the models embedded in the decisional agents and each decisional agent is not aware of the presence of the other decisional agents, we ensure the flexibility of adding new decisional agents without modifying the rest of the system. On the other hand, this means that the negotiation among them must be carried out by means of an external mediator. The way in which the decisional agents negotiate an acceptable compromise with the mediation of the equalizer component of the knowledge blackboard agent is the core of the functioning of the glucose–insulin metabolism control anthropic agency and is extensively described in Section 4.3.

4.2.3. The actuator agent

The actuator agent implements the following actuation function: $A(\bar{I}(t), \bar{G}(t), \Delta\bar{G}(t), \bar{A}(t)) = \boldsymbol{a}(t)$ with $\boldsymbol{a}(t) = (\Delta I_a(t))$, where $\Delta I_a(t)$ is the planned variation of insulin to accomplish at time t. We assume that the actuator agent is connected to an insulin

infusion pump. Therefore, the insulin concentration is the only quantity the actuator agent can directly vary and, moreover, $\Delta I_a(t)$ is always positive (since the actuator is an insulin infusion pump).

4.3. The negotiation mechanism

We now illustrate how the decisional agents negotiate their decisions with the mediation of the equalizer component of the knowledge blackboard agent. Moreover, we describe how the agreed decisions are translated into actions by the actuator agent. A preliminary and shorter description of the negotiation mechanism presented in this section can be found in [2].

4.3.1. The algorithm for the decisional agents

A decisional agent, by means of an heuristic gradient descent technique, identifies a set of desirable target states that minimise the potential values of the model embedded the decisional agent. In this way, a decisional agent j, knowing its current state $\boldsymbol{p}_j(t) = (x_j^1(t), x_j^2(t), \ldots, x_j^{n_j}(t))$ (as read from the parameters blackboard), determines a set of possible target states, $\{\bar{\boldsymbol{p}}_j(t+1)\}$, where $\bar{\boldsymbol{p}}_j(t+1) = (\bar{x}_j^1(t+1), \bar{x}_j^2(t+1), \ldots, \bar{x}_j^{n_j}(t+1))$. To select a single target state that will constitute its proposed decision, the decisional agent j calculates the cost of the variation of each parameter p_j^h from the current state to a target state as

$$C(p_j^h) = C_j^h \, \Delta x_j^h = C_j^h |\bar{x}_j^h(t+1) - x_j^h(t)|$$

The unitary cost C_j^h of the parameter p_j^h is the sum of two elements: $C_a(p_j^h)$, which is determined by the actuator agent that acts on p_j^h (as explained later), and $C_n(p_j^h)$, which is determined by the equalizer component during the negotiation process. The structure of the communication of these costs is shown in Fig. 5. $C_a(p_j^h)$ is the actuation cost, namely, the cost associated to the physical variation of the parameter $p^h(t)$. $C_n(p_j^h)$ is the negotiation cost: the measure of the difficulty to change the parameter p_j^h according to the desires of the other decisional agents. In other words, $C_n(p_j^h)$ is a measure of how much can be granted to

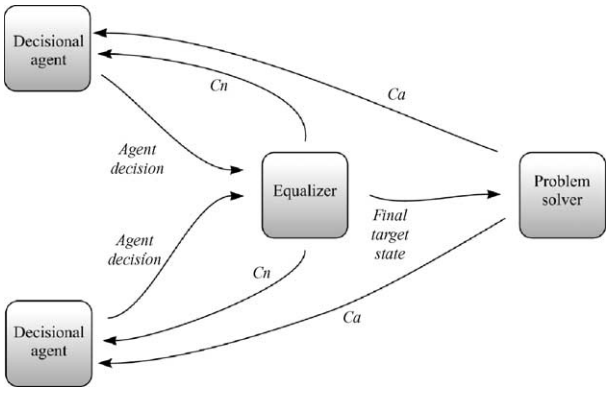

Fig. 5. A schematic representation of the messages involved in the negotiation mechanism.

the decisional agent j on parameter p_j^h when the proposed variations of the other decisional agents on the same parameter are taken into account. Hence, from the previous discussion we have: $C_j^h = C_a(p_j^h) + C_n(p_j^h)$. We also note that $|\bar{x}_j^h(t+1) - x_j^h(t)|$ can be considered as a sort of variation cost.

The global cost (for the decisional agent j) of reaching the target state $\bar{\boldsymbol{p}}_j(t+1)$ from the current state $\boldsymbol{p}_j(t)$ is given by

$$C(\boldsymbol{p}_j) = \sum_{h=1}^{n_j} C(p_j^h) = C_j^1 \Delta x_j^1 + C_j^2 \Delta x_j^2 + \cdots + C_j^{n_j} \Delta x_j^{n_j}$$

The decisional agent j then selects (from the set of identified target states that minimise the potential values) the point with the minimum cost: this is its proposed target state. Of course, since the current state changes and since the costs change during the negotiation (because the $C_n(p_j^h)$ change), the target point proposed by a decisional agent j may change over time.

Every parameter value of a proposed target point has an associated weight as explained in Section 4.2.2. This means that the vector of decisions $\boldsymbol{d}_j$ produced by the decisional agent j is given by

$$(\langle \bar{x}_j^1(t+1), W_j^1(t+1)\rangle, \langle \bar{x}_j^2(t+1), W_j^2(t+1)\rangle, \ldots, \langle \bar{x}_j^{n_j}(t+1), W_j^{n_j}(t+1)\rangle)$$

Each weight $W_j^h(t+1)$ is the product of two factors. The first one depends on the difference between the potential $v(x_j^h(t))$ of the current value of p_j^h and the potential $v(\bar{x}_j^h(t+1))$ of the proposed value of p_j^h; specifically the first factor is $1 + |v(\bar{x}_j^h(t+1)) - v(x_j^h(t))|$. We note that $v(x_j^h(t)) = v(\boldsymbol{p}_j(t))$ and $v(\bar{x}_j^h(t+1)) = v(\bar{\boldsymbol{p}}_j(t+1))$. The second factor is the value $W_j(t+1)$ that represents the importance of the decisional agent j. The idea behind the introduction of the importance $W_j(t+1)$ is that the physiological processes models embedded in decisional agents have different importance. For example, by setting the importance weights it is possible to give higher priority to the control of vital functions than to the control of peripheral functions. The value of $W_j(t+1)$ is variable according to the current state of the system. In our experimental activity, the importance of the two decisional agents varies according to the values shown in Fig. 6. It is easy to see that the importance of the first decisional agent, which is related to the food absorbtion, is higher than that of the second decisional agent, which is related to physical activity. This reflects the fact that the main problem of a diabetic patient is the insulin response when the patient eats. To summarise, $W_j^h(t+1) = (1 + |v(\bar{x}_j^h(t+1)) - v(x_j^h(t))|)W_j(t+1)$ (we note that all $W_j(t+1)$ are equal, for all h). On the one hand, $|v(\bar{x}_j^h(t+1)) - v(x_j^h(t))|$ is a measure of how far the parameter p_j^h is from the optimum value, according to the decisional agent j. On the other hand, $W_j(t+1)$ is a measure of how important is the physiological function controlled by the decisional agent j.

4.3.2. The algorithm for the equalizer component

The equalizer component of the knowledge blackboard agent collects from the decisional agents their proposed decisions. Then, it calculates for each parameter p^h the weighted average of the proposed target values for that parameter. In this average, the weight of the value $\bar{x}_j^h(t+1)$ is $W_j^h(t+1)$. Therefore, the equalizer component, for each

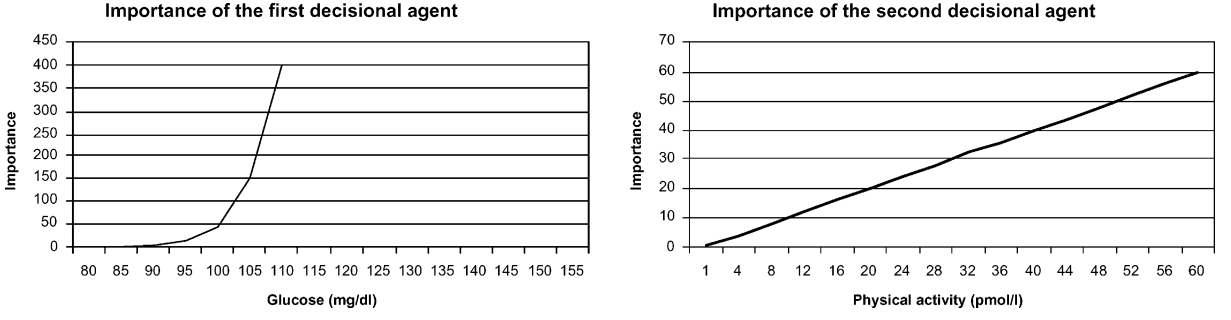

Fig. 6. The importance values W_1 (left) and W_2 (right) of the two decisional agents employed in our experimental activity.

parameter p^h, determines the new value of p^h as the weighted average of the proposed values:

$$\bar{x}^h(t+1) = \frac{\sum_{j=1}^{J_h} \bar{x}_j^h(t+1) W_j^h(t+1)}{\sum_{j=1}^{J_h} W_j^h(t+1)}$$

where J_h is the number of decisional agents operating on h.

The equalizer component determines also the cost $C_n(p_j^h)$ for each decisional agent j. This cost accounts for the difficulty to reach the value proposed by j due to the other (weighted) proposals. $C_n(p_j^h)$ is simply calculated as $|\bar{x}^h(t+1) - \bar{x}_j^h(t+1)|$. High values of $C_n(p_j^h)$ mean that the proposed value $\bar{x}_j^h(t+1)$ is far from the other proposed values for p^h and that the decisional agent j is not in accordance with the other decisional agents about p^h. The costs $C_n(p_j^h)$ are then communicated to the decisional agents that can change their proposed points (as previously explained and as shown in Fig. 5).

The equalizer performs the described operations for each parameter p^h a number of times before the end of a 30 s time interval. Thus during this negotiation time, the target states proposed by decisional agents are changed according to new negotiation costs. We recall that, since the agents are asynchronous, the frequencies of parameters readings (by decisional agents) and of decision making (by the equalizer component) may be different.

We note that the final result, namely, the set of values $\{\bar{x}^h(t+1)\}$, represents a state that is not the optimum for every decisional agent (i.e. for every physiological model), but it is somehow the optimum for social welfare of the system. The decisions of some decisional agents (for instance, the ones with lower intrinsic importance) are sacrificed for the global goodness of the system.

4.3.3. The algorithm for the actuator agent

Every time the equalizer determines a new set of values $\{\bar{x}^h(t+1)\}$ for the parameters $\{p^h\}$, these values are sent to the actuator agents that can perform action to change the values of $\{p^h\}$ (Fig. 5). We recall that we made the assumption (see Section 3) that the actuator agents can perform only different actions; this means that there cannot be two actuator agents that can operate to vary the same parameter. Each actuator agent includes a problem solver that finds the actions that have to be carried on to reach the value $\bar{x}^h(t+1)$ for the parameter p^h. The actuator agent plans a sequence of actions that brings to $\bar{x}^h(t+1)$ starting from the current value of $x^h(t)$ read from the parameters blackboard (the information flow between the parameters blackboard and the actuator agents in not explicitly shown in Fig. 3). The planned actions are then modified to account for the dynamics that are currently undergoing as consequence of the previously performed actions. The resulting modified plan is then executed exploiting the actuators.

From the model of actions, the problem solver component of the actuator agent also calculates the actuation costs $C_a(p_j^h)$ and sends them to the decisional agents (see Fig. 5). In our experimental activity the actuation costs (we note that not the actual values of these costs, but their relative rates are significant for the negotiation) have been determined as follows: a positive variation of insulin has cost 1, a negative variation of insulin has cost 3, a positive variation of glucose has infinite cost, and a negative variation of glucose has cost 6. These costs have been set taking into account the fact that, in the glucose–insulin

metabolism process, the range of insulin variation is much larger than the range of glucose variation and thus it is better to vary insulin level than glucose level. We remark that, although the actuator agent cannot lower the insulin (see Section 4.2.3), a negative variation of insulin has not infinite cost: this allows the decisional agents to explore all their spaces of states. The parameters whose variation has not any meaning, ΔG and A, have infinite actuation costs.

4.3.4. Discussion on the negotiation mechanism

An example of a typical negotiation that occurs in our anthropic agency is reported in Fig. 7. We have tested the negotiation mechanism as an independent subsystem of the anthropic agency. The experiments on the whole anthropic agency are reported in Section 5. We built three synthetic models and we embedded them in the decisional agents. The three models are defined on two parameters: x_1 and x_2. The models are reported in Fig. 8 (left). The importance W_j of the three decisional agents have been set equal to a fixed constant. Also all actuation costs $C_a(p_j^h)$ have been set equal to a fixed constant. In this way, the final target states generated by the equalizer depend only on the starting states and on the evolution of negotiation costs. During the negotiation process, we registered the states generated by the equalizer before the end of the time interval. Such set of states generated in a simulation is shown in Fig. 8 (right) (other simulations with different starting states produce similar results). From Fig. 8 (right), it appears that the generated points lie all in the region of space in which all three models have good potential values. This means that the proposed negotiation mechanism is effective in finding an agreement among possibly contrasting decisions.

Despite the experimental validation, and the fact that the negotiation process always converged in our tests, we have not any theoretical proof of the convergence of this negotiation mechanism. Its theoretical evaluation is one of the issues we will address in the future work.

According to the framework presented in [24], we summarise the contributions of this section. We have described both the agents decision making models and the rules governing the interaction that allows agents to agree on the target state to reach. The negotiation mechanism we adopted belongs to the class of data fusion paradigms [10,32].

4.4. Implementation details

The implementation of the anthropic agency required the use of a programming language that would support networking applications and parallel processes. The choice has fallen on the programming language Java [5]. The problem solvers and the other reasoning components of the agents have been coded in Jess [18].

All the agents have a common structure of three interfaces, used to connect and exchange information with other agents or with sensors and actuators. The agents are made by parallel threads. All agents have a main thread, the agent manager, that starts and manages all the other threads of the agent. The agent manager initialises and subscribes the agent to the blackboards and majordomo agent. The user can ask the agent manager services to update the agent threads; this makes the system very flexible since the user can both change the composition of the anthropic agency, introducing a new agent, and update the functionality of the single agents.

Current state at time T: $I = 25.5 pmol/l, G = 98.5 mg/dl, \Delta G = 0.4 mg/dl, A = 30 pmol/l$
Importance of decisional agents $W_1(T+1) = 48$ and $W_2(T+1) = 30$

Decisional agent 1	**Decisional agent 2**
possible target states $\bar{\mathbf{p}}_1 = (\bar{I}_1, \bar{G}_1, \bar{\Delta G}_1)$	possible target states $\bar{\mathbf{p}}_2 = (\bar{I}_2, \bar{G}_2, \bar{A}_2)$
$\bar{\mathbf{p}}_{1,1} = (28.5, 92.5, 0.4)$	$\bar{\mathbf{p}}_{2,1} = (25.5, 97.5, 30)$
$\bar{\mathbf{p}}_{1,2} = (30.5, 92.5, 0.4)$	$\bar{\mathbf{p}}_{2,2} = (25.5, 98.5, 30)$
$\bar{\mathbf{p}}_{1,3} = (34.5, 93.5, 0.4)$	$\bar{\mathbf{p}}_{2,3} = (25.5, 99.5, 30)$

for all these points: $|v(\bar{\mathbf{p}}_{a,b}) - v(\text{current state at time } T)| = 12$ ($a \in \{1,2\}$ and $b \in \{1,2,3\}$)

STEP α (initially all the negotiation costs are 0)

$C(\bar{\mathbf{p}}_{1,1}) = (1+0)\cdot 3 + (6+0)\cdot 6 + 0 = 39$ $\quad C(\bar{\mathbf{p}}_{2,1}) = 0 + (6+0)\cdot 1 + 0 = 6$
$C(\bar{\mathbf{p}}_{1,2}) = (1+0)\cdot 5 + (6+0)\cdot 6 + 0 = 41$ $\quad C(\bar{\mathbf{p}}_{2,2}) = 0 + 0 + 0 = 0$
$C(\bar{\mathbf{p}}_{1,3}) = (1+0)\cdot 9 + (6+0)\cdot 5 + 0 = 39$ $\quad C(\bar{\mathbf{p}}_{2,3}) = 0 + (\infty+0)\cdot 1 + 0 = \infty$
proposed state $(34.5, 93.5, 0.4)$ (ties are broken randomly) $\quad$ proposed state $(25.5, 98.5, 30)$

The equalizer component calculates

$$\bar{I}(T+1) = \frac{(34.5\cdot((1+12)\cdot 48)) + (25.5\cdot((1+12)\cdot 30))}{(1+12)\cdot 48 + (1+12)\cdot 30} = 31$$

$$\bar{G}(T+1) = \frac{(93.5\cdot((1+12)\cdot 48)) + (98.5\cdot((1+12)\cdot 30))}{(1+12)\cdot 48 + (1+12)\cdot 30} = 95.4$$

STEP β

$C(\bar{\mathbf{p}}_{1,1}) = (1+2.5)\cdot 3 + (6+2.9)\cdot 6 + 0 = 63.9$ $\quad C(\bar{\mathbf{p}}_{2,1}) = 0 + (6+2.1)\cdot 1 + 0 = 8.1$
$C(\bar{\mathbf{p}}_{1,2}) = (1+0.5)\cdot 5 + (6+2.9)\cdot 6 + 0 = 60.9$ $\quad C(\bar{\mathbf{p}}_{2,2}) = 0 + 0 + 0 = 0$
$C(\bar{\mathbf{p}}_{1,3}) = (1+3.5)\cdot 9 + (6+1.9)\cdot 5 + 0 = 80$ $\quad C(\bar{\mathbf{p}}_{2,3}) = 0 + (\infty+4.1)\cdot 1 + 0 = \infty$
proposed state $(30.5, 92.5, 0.4)$ $\quad$ proposed state $(25.5, 98.5, 30)$

The equalizer component calculates

$$\bar{I}(T+1) = \frac{(30.5\cdot((1+12)\cdot 48)) + (25.5\cdot((1+12)\cdot 30))}{(1+12)\cdot 48 + (1+12)\cdot 30} = 28.6$$

$$\bar{G}(T+1) = \frac{(92.5\cdot((1+12)\cdot 48)) + (98.5\cdot((1+12)\cdot 30))}{(1+12)\cdot 48 + (1+12)\cdot 30} = 94.8$$

STEP γ

$C(\bar{\mathbf{p}}_{1,1}) = (1+0.1)\cdot 3 + (6+2.3)\cdot 6 + 0 = 53.1$ $\quad C(\bar{\mathbf{p}}_{2,1}) = 0 + (6+2.7)\cdot 1 + 0 = 8.7$
$C(\bar{\mathbf{p}}_{1,2}) = (1+1.9)\cdot 5 + (6+2.3)\cdot 6 + 0 = 64.3$ $\quad C(\bar{\mathbf{p}}_{2,2}) = 0 + 0 + 0 = 0$
$C(\bar{\mathbf{p}}_{1,3}) = (1+5.9)\cdot 9 + (6+1.3)\cdot 5 + 0 = 98.6$ $\quad C(\bar{\mathbf{p}}_{2,3}) = 0 + (\infty+4.7)\cdot 1 + 0 = \infty$
proposed state $(28.5, 92.5, 0.4)$ $\quad$ proposed state $(25.5, 98.5, 30)$

The equalizer component calculates

$$\bar{I}(T+1) = \frac{(28.5\cdot((1+12)\cdot 48)) + (25.5\cdot((1+12)\cdot 30))}{(1+12)\cdot 48 + (1+12)\cdot 30} = 27.3$$

$$\bar{G}(T+1) = \frac{(92.5\cdot((1+12)\cdot 48)) + (98.5\cdot((1+12)\cdot 30))}{(1+12)\cdot 48 + (1+12)\cdot 30} = 94.8$$

In the following steps before the $30s$ timeout, the values $\bar{I}(T+1)$ and $\bar{G}(T+1)$ are stabilized at 27.3 and 94.8, respectively

Fig. 7. An example of a negotiation that occurs in our anthropic agency.

The skeleton of the anthropic agency is constituted by the two blackboard agents and by the majordomo agent. The other agents, to be inserted in the anthropic agency, have to subscribe themselves to these entities offering and requiring sets of services. The peer-to-peer network connections among them are based on RMI; this means that the agents can

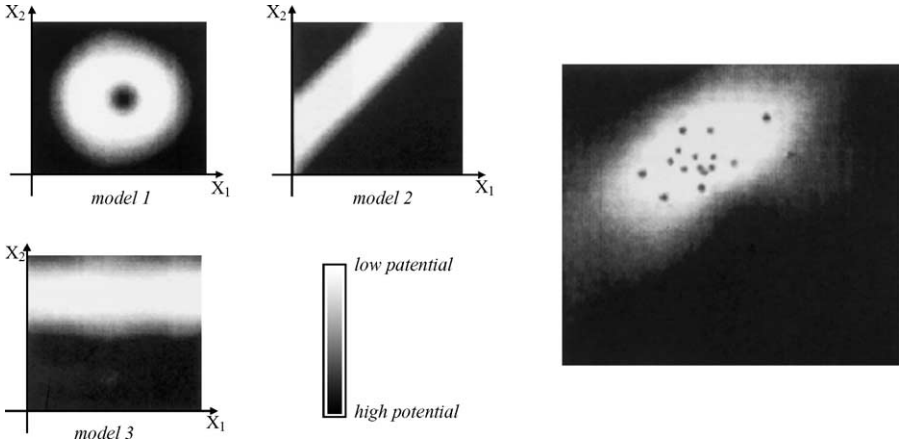

Fig. 8. The three synthetic models for the experimental test of the negotiation mechanism, the points in lighter regions are "good", while the points in darker regions are "bad" (left); the states generated during the negotiation mechanism in the space obtained by superposition of the three models (right).

run on different processors. The role of an agent depends on whether it is asking or supplying a service in that given moment. Each blackboard agent is constituted by two parallel threads that manage the information exchange through the shared memory. Moreover, the knowledge blackboard agent includes a set of threads that implement the equalizer component. The majordomo agent is a process that allows users or other processes to connect to the anthropic agency, for example, to update an agent.

In the extractor agents, other threads (besides the agent manager) periodically sample and process the signals coming from the sensors. These threads produce the parameters values that are sent to the parameters blackboard agent. The actuator and the decisional agents include threads to get periodically parameters from the parameters blackboard. Each thread is specific for a single parameter; in this way the agent is able to get different parameters with different frequencies and to stop or start the reading of a parameter without any influence on the others. The decisional agents have also a model manager thread and a negotiation thread. The actuator agents activate threads that plan the actions to be performed when an agreed-upon decision is found in the knowledge blackboard.

5. Experimental results

We have tested our implementation of anthropic agency in different situations to evidence the flexibility offered by the system. In this section, we report and comment some of the most significant experiments we carried out. During the experiments illustrated here, the negotiation and actuation costs have been set according to Sections 4.3.2 and 4.3.3 and the importance of the two decisional agents has been set as in Fig. 6.

Firstly we demonstrate that the employed simulation system works properly. The curves of Fig. 9 show that the insulin and the glucose curves produced by the simulation system while simulating a normal person slightly oscillate around the normal basal values: about

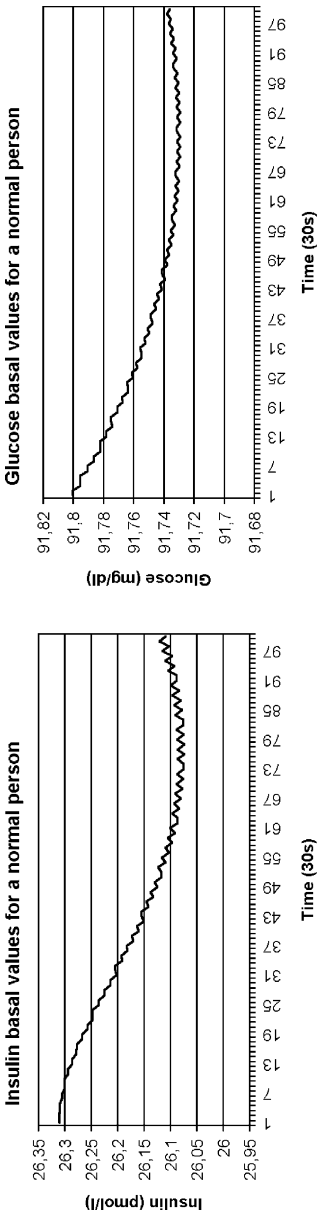

Fig. 9. The insulin and glucose levels in a normal person.

26.2 ± 0.15 pmol/l for the insulin level and about 91.7 ± 0.06 mg/dl for the glucose level. The small-entity oscillations around these values are due to the internal dynamics of the simulator. In a similar way, the curves of Fig. 10 are produced by the simulation system while simulating a diabetic patient. They correctly present insulin and glucose basal values that are, respectively, slightly less (18.8 ± 0.1 pmo/l and slightly more (98.2 ± 0.1 mg/dl) than the basal values of a normal person, in accordance with the behaviour of real diabetic patients [34].

The main problem in the diabetic pathology is the insulin response after a meal, because it is when the glucose concentration reaches the maximum value. In fact, Fig. 11 represents a food ingestion curve and the black curves of Fig. 12 show the corresponding response (as resulting from the simulation system) of a normal person. In Fig. 12 (dark grey curves) we report also the response to the same food ingestion curve of a diabetic patient. It is clear that the response of a person affected by diabetic pathology relevantly differs from that of a normal person. The light grey curves of Fig. 12 show how the anthropic agency in which we inserted only the first decisional agent (that reduces the glucose concentration during food absorbtion, see Section 4.2.2) can effectively regulate the insulin and the glucose levels in a diabetic patient eating according to the curve of Fig. 11. The regulation activity of the anthropic agency brings the glucose–insulin metabolism of an eating diabetic patient close to that of an eating normal person (compare the black and the light grey curves of Fig. 12). This shows the effectiveness of the control action of the anthropic agency with a single decisional agent and thus with a trivial negotiation activity. The high-frequency oscillations of the insulin curve are due to the asynchrony between the simulation system and the actuator agent.

To demonstrate the effect of the negotiation mechanism on the regulation activity of anthropic agency, we introduce a new disturb in the simulation system. We suppose that the diabetic patient is underdoing an intense physical activity (such as a long run). The corresponding input curve is represented in Fig. 13 and the response of a normal person to that curve (obtained by the simulation system) is reported by black curves in Fig. 14. The dark grey curves of Fig. 14 show that the anthropic agency with only the decisional agent that regulates the glucose–insulin metabolism with respect to food absorbtion is not able to correctly regulate the insulin and glucose levels in presence of an intense physical activity. With the insertion of the second decisional agent, which is specifically devoted to regulate the glucose–insulin metabolism with respect to physical activity, the control activity performed by the anthropic agency is enhanced, as illustrated by the light grey curves of Fig. 14. This shows that the negotiation among the two decisional agents is effective and finds a reasonable compromise that brings the insulin and glucose curves of a diabetic patient who performs physical activity close to those of a normal person (compare the black and the light grey curves of Fig. 14).

In Fig. 15 we report the insulin and glucose curves of a diabetic patient who, at the same time, is absorbing food and doing a physical activity. This implies a very complex control activity since the two decisional agents have contrasting goals. The first one tries to lower the glucose level while responding to the food ingestion and the second one tries to keep constant the glucose level for sustaining the physical activity. Since the interval in which the physical activity input is active is shorter than the interval in which the food absorbtion input is active, we report only the portions of the curves in which both input are active

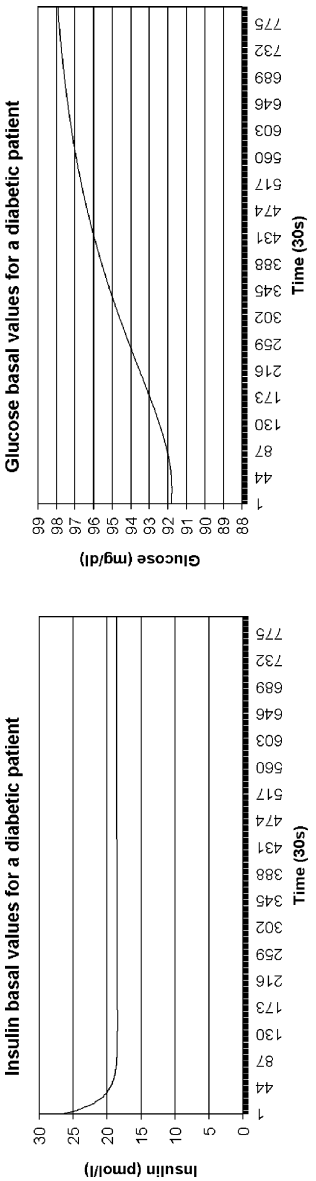

Fig. 10. The insulin and glucose levels in a diabetic patient.

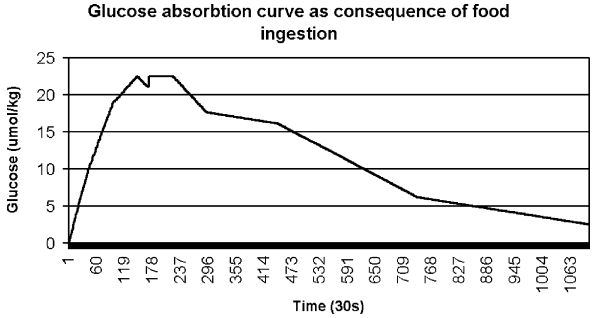

Fig. 11. The curve representing the food absorbtion used in our experiments.

(it makes no much sense to expose a diabetic patient to a one hour and half intense physical activity after a meal). The curves show that the negotiation mechanism between the two decisional agents works properly also in this case and brings the two decisional agents to reach an agreement. In fact, the insulin curve is between those (light grey curves) of Figs. 12 and 14.

Finally we present an experiment that evidences the role of the decisional agents importance. Fig. 16 displays the effects of the control action of the anthropic agency in

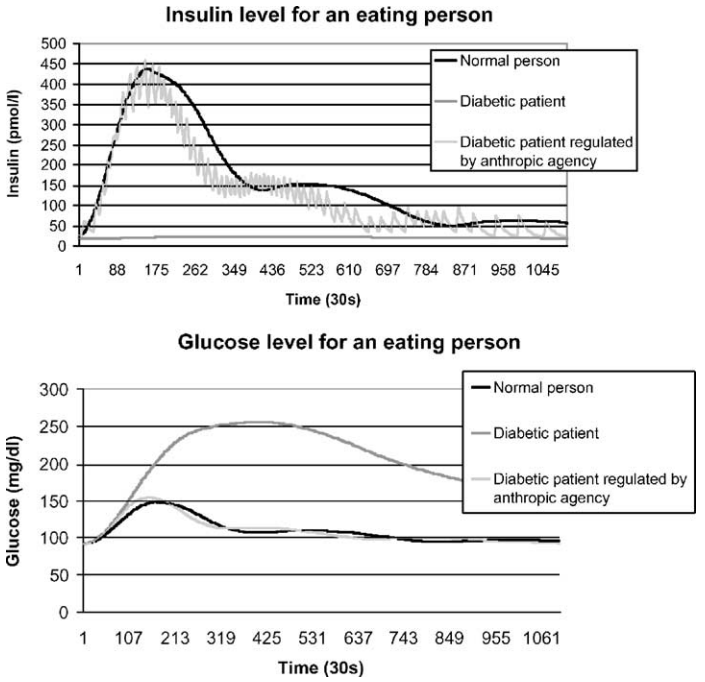

Fig. 12. The insulin and glucose curves of a normal person, of a diabetic patient, and of a diabetic patient subject to the regulation activity of the anthropic agency with a single decisional agent, when eating according to the curve of Fig. 11.

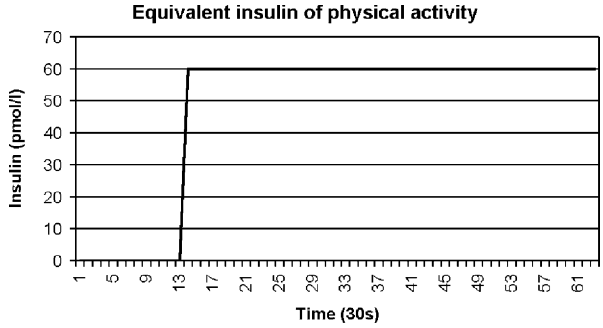

Fig. 13. The curve representing the physical activity used in our experiments.

which the two decisional agents have the same importance on a diabetic patient performing a physical activity. More precisely, at the beginning of the simulation, only the second decisional agent is active, then, at time 21 (times 30 s) the first decisional agent is activated with the same importance of the second one. From the oscillations of the insulin curve it

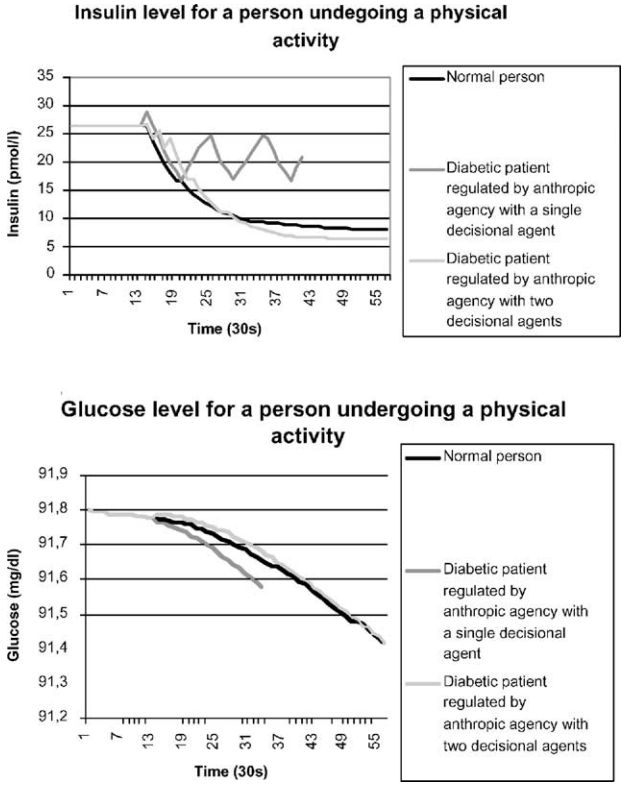

Fig. 14. The insulin and glucose curves of a normal person, of a diabetic patient subject to the regulation activity of the anthropic agency with a single decisional agent, and of a diabetic patient subject to the regulation activity of the anthropic agency with two decisional agent, when undergoing the physical activity of Fig. 13.

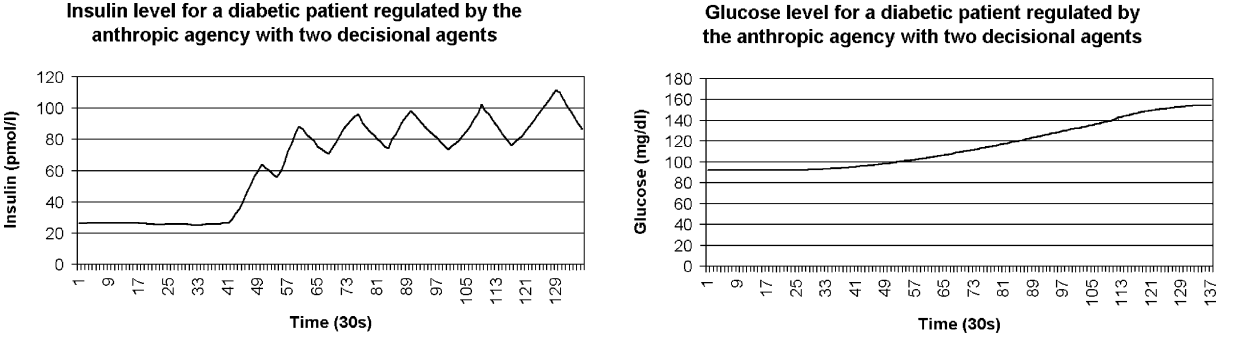

Fig. 15. The insulin and glucose curves of a diabetic patient when absorbing food according to the curve of Fig. 11, undergoing the physical activity of Fig. 13 and subject to the regulation activity of the anthropic agency with two decisional agents with the same importance.

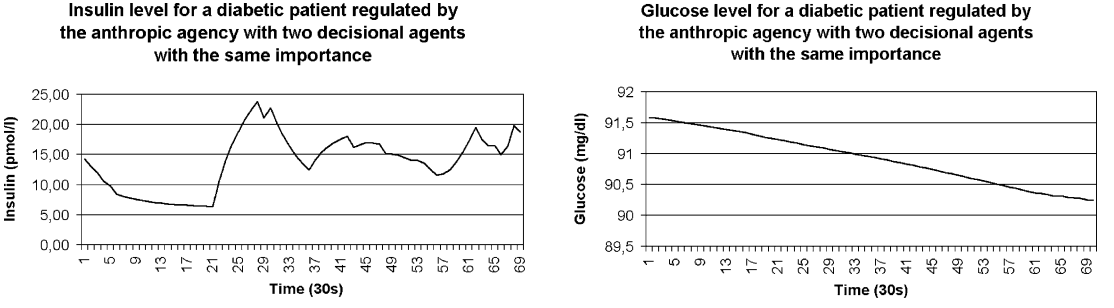

Fig. 16. The insulin and glucose curves of a diabetic patient when undergoing the physical activity of Fig. 13 and subject to the regulation activity of the anthropic agency with two decisional agents with the same importance.

appears the contrasting actions of the two decisional agents that could not reach an agreement on the insulin value. As a consequence, we note that the insulin curve of Fig. 16 is quite worst than that of Fig. 14 (light grey) that was obtained with the importance as in Fig. 6. Moreover, the insulin curve of Fig. 16 is similar to that of Fig. 14 (dark grey), with the difference that the oscillations of the former one are around lower insulin values because of the action of the second decisional agent. This demonstrates that the choice of the importance of the decisional agents as in Fig. 6 was reasonable both because it reflects the current body of knowledge on diabetes (the food ingestion is the most critical moment for a diabetic patient) and because it brings to acceptable experimental results.

6. Flexibility of anthropic agency

The major advantages of the anthropic agency paradigm are summarised in the property of *flexibility*. More precisely, an anthropic agency-based control system is flexible in three dimensions.

- *Towards the user*, since the flexible adaptable and robust negotiation among the agents allows the use of the same system for different users, or for the same user in different times. In fact, the decisional agents and the equalizer component are independent from the user. The information about the user physiology influences only the actuator agents. This means that when the anthropic agency is applied to another patient, the only software components that need to be changed are those of actuator agents. The adaptability of the anthropic agency toward the user can be improved by employing learning techniques to tune the user-dependent parameters. However, this possibility has not been yet explored in our experimental activity.
- *Towards the designer*, since the system is easy to build, maintain, and update. Each agent of the control system is implemented as a set of software components and the agents can run on different processors connected together by a (possibly wireless) communication network (see Section 4.4). Therefore, the system can be dynamically updated by inserting new agents or by modifying the interaction paradigm, also while the system is working. In this way, new models may enrich the system (which presents a variable topology [8]). These models may either represent processes already described in the agency or models of new processes. In the first case, different models of the same phenomenon describing different aspects of it enable to obtain a very precise description of the phenomenon and of its aspects. In the second case, the system is enriched and its potential is expanded. Our experimental activity displayed that, by adding a new decisional agent (the one related to physical activity) to the anthropic agency, the performance of the system is improved (as illustrated in Fig. 14).
- *Towards the application*, since the same general architecture of anthropic agency can be employed for addressing different applications. This is a still unexplored possibility. We are currently working to develop a new anthropic agency implementation that address the problem of the setting the pace-makers frequency on the basis of the values of a set of parameters read from sensors. This new implementation of anthropic agency will represent an innovation with respect to the current pace-makers frequency regulators

that are either manual (the physician sets the frequency by hand on the basis of his experience) or dependent on a single signal (e.g. the values returned by a piezoelectric crystal sensor). We aim to demonstrate that the same general architecture applies to both application fields: glucose–insulin metabolism and heart pumping.

7. Conclusions

In this paper we have presented a multiagent architecture, called anthropic agency, for modelling and controlling physiological processes. We have illustrated the structure and the properties of the architecture with particular emphasis on the negotiation paradigm, since it constitutes the core of the non-destructive interaction among agents. The validity of the proposed paradigm has been experimentally verified by developing and implementing an anthropic agency for regulating the human glucose–insulin metabolism processes.

The discussion on the future research work must start from the consideration that the definition of the anthropic agency architecture and of its negotiation mechanism is only the first step of a more comprehensive project that aims to employ multiagent techniques to control physiological processes. We believe that the adoption of multiagent systems can bring a number of advantages, because of their ability to incorporate incomplete and partial models of phenomena. The implementation of the anthropic agency presented in this paper, devoted to glucose–insulin metabolism, may be improved by using learning techniques to tune the user-dependent parameters of actuator agents. Moreover, further work is needed to formally investigate the properties of the negotiation mechanism we employ. The next big step in the global project will be the adoption of anthropic agency to address new applications. In this direction, we are already cited our work in developing (in cooperation with some biomedical schools) a new anthropic agency implementation for determining the pace-maker frequency. The long-term goal of the project is the implementation of the anthropic agency in wearable computers and robots that can be employed not only to control the physiological processes on real persons, but also to monitor physiological values, to diagnose pathological states, and to acquire, process, and communicate data for telemedicine. In this perspective, it is important to investigate how the same architecture could cope both with urgent regulation tasks and with less impelling monitoring and diagnostic tasks that require reactive and plan-based behaviours, respectively. Other interesting and still mainly unexplored research lines involve the integration of the anthropic agency-based systems with other ubiquitous computational systems (such as domotic and urban agents) by means of some interoperability framework.

Acknowledgements

The authors are glad to thank the contributions of Michele Bassanelli, Martino Noris, and Nicoló Soresina and the kind cooperation of Claudio Cobelli and Gianluca Nucci. We also thank the two reviewers for their valuable suggestions.

References

[1] Aarsten A, Brugali D, Menga G. Designing concurrent and distributed control system. Commun ACM 1996;39(10):50–8.

[2] Amigoni F, Gatti N, Somalvico M. A multiagent interaction paradigm for physiological process In: Castelfranchi C, Lewis Johnson W, editors. Proceedings of the First International Joint Conference on Autonomous Agents and Multiagent Systems (AAMAS2002), Part 1, 2002 July 17–19; Bologna, Italy. New York: ACM. p. 215–6.

[3] Amigoni F, Schiaffonati V, Somalvico M. A multilevel architecture of creative dynamic agency. Foundations Sci 2000;5(2):157–84.

[4] Amigoni F, Somalvico M, Zanisi D. A theoretical framework for the conception of agency. Int J Intelligent Syst 1999;14(5):449–74.

[5] Arnold K, Gosling J, Holmes D. The Java programming language. Boston, MA: Addison-Wesley; 2000.

[6] Balduzzi F, Brugali D. A hybrid software agent model for decentralized control. In: Proceedings of the IEEE International Conference on Robotics and Automation, 2001; Seoul, Korea. New York: IEEE Press. p. 836–41.

[7] Berger MP, Meyer RA, Miller PL. Combining statistical, rule based and physiological model based methods to assist the management of diabetes mellitus. Comput Biomed Res 1990;23:346–57.

[8] Brennan RW, Balasubramanian S, Norrie DH. A dynamic control architecture for metamorphic control of advanced manufacturing systems. In: Gopalakrishnan B, Murugesan S, Struger O, Zeichen GD, editors. Proceedings of the International Symposium on Intelligent Systems and Advanced Manufacturing, SPIE, Pittsburgh, PA, USA. Proc SPIE 1997;3203:213–23.

[9] Candas B, Radziuk J. An adaptive plasma glucose controller based on nonlinear insulin/glucose model. IEEE Trans Biomed Eng 1994;41:116–24.

[10] Chaudron L, Erceau J, Trousse B. Co-operative decisions and actions in multiagent worlds. In: Proceedings of the IEEE International Conference on Systems, Man and Cybernetics, vol. 3, 1993; Le Touquet, France. New York: IEEE Press. p. 626–9.

[11] Cobelli C, Nucci G, Del Prato S. A physiological simulation model of the glucose–insulin system. In: Blanchard SM, Eckstein EC, Fouke JM, Nerem RM, Yoganathan AP, editors. Proceedings of the BMES/EMBS Conference, 1999, Oct 13–16; Atlanta, GA, USA. New York: IEEE Press.

[12] Conry SE, Meyer RA, Lesser VR. Multistage negotiation in distributed planning. In: Bond AH, Gasser L, editors. Readings in distributed artificial intelligence. San Matteo, CA, USA: Morgan Kaufmann; 1988. p. 367–84.

[13] Davis WJ. The distributed intelligent control of complex systems. In: Meech JA, Veiga MM, Smith MH, LeClair SR, editors. Proceedings of the Second International Conference on Intelligent Processing and Manufacturing of Materials, vol. 1, 1999; Honolulu, HI, USA. New York: IEEE Press. p. 615–21.

[14] Dorman FD, Wigness BD, Rohde TD, Beling WL, Buchwald H. A new spring-driven implantable drug infusion pump. In: Kim Y, Spelman FA, editors. Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 1989; Seattle, WA, USA. New York: IEEE Press. p. 1538–9.

[15] Erman LD, Hayes-Roth F, Terry A, Hayes-Roth B. Distributed intelligent control and management: concepts, methods and tools for developing dicam applications. In: Fourth International Conference on Software Engineering and Knowledge Engineering, 1992; Capri, Italy. New York: IEEE Press.

[16] Ferber J. Multiagent systems: an introduction to distributed artificial intelligence. Harlow, UK: Addison-Wesley; 1999.

[17] FIPA, Communicative act library specification. Technical report, Foundation for Intelligent Physical Agents, 2000, http://www.fipa.org.

[18] Friedman-Hill E. Java expert system shell. Sandia National Laboratories, http://www.herzberg.ca.sandia.-gov/jess/.

[19] Fu KS, Gonzales RC, Lee CSG. Robotics: control, sensing, vision, and intelligence. New York: McGraw-Hill; 1987.

[20] Goldberger AL, West BJ. Chaos in physiology: health or disease. In: Holteon A, Olsen LF, editors. Chaos in biological systems. New York: Plenum Press; 1987. p. 1–5.

[21] Hayes-Roth B, Larsson JE. Guardian: an intelligent autonomous agent for medical monitoring and diagnosis. IEEE Intelligent Syst 1998(January/February):58–64.
[22] Jennings NR. On agent-based software engineering. Artificial Intelligence 2000;117:277–96.
[23] Jennings NR. An agent-based approach for building complex software systems. Commun ACM 2001;44(4):35–41.
[24] Jennings NR, Faratin P, Lomuscio AR, Parsons S, Sierra C, Wooldridge M. Automated negotiation: prospects, methods and challenges. Int J Group Decision Negotiation 2001;10(2):199–215.
[25] Lee JJ, Norris II WD, Fishwick PA. An object-oriented multimodel approach to integrate planning, intelligent control and simulation, In: Proceedings of the Fourth Annual Conference on AI, Simulation, and Planning in High Autonomy Systems, 1993; Tucson, AZ, USA. New York: IEEE Press. p. 267–73.
[26] Nii HP. Blackboard systems. 2. Blackboard application systems. AI Magazine 1986;3(VII):82–106.
[27] Nii HP. Blackboard systems: the blackboard model of problem solving and the evolution of blackboard architectures. AI Magazine 1986;2(VII):38–53.
[28] Norrie DH, Shen W. Agent based systems for intelligent manufacturing: a state of the art survey. Knowledge Information Syst 1999;1(2):129–56.
[29] Omicini A, Zambonelli F. Coordination for internet application development. Autonomous Agents Multiagent Syst 1999;2(3):251–69.
[30] Parker RS, Doyle III JF, Harting JE, Peppas NA. Model predictive control for infusion pump insulin delivery. In: Proceedings of the 18th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 1997; Chicago, IL, USA. New York: IEEE Press. p. 1822–3.
[31] Parker RS, Gatzke EP, Doyle III JF. Advanced model predictive control for type I diabetic patient blood glucose control. In: Proceedings of the American Control Conference, 2000 June; Chicago, IL, USA. New York: IEEE Press.
[32] Rantilla AK, Budescu DV. Aggregation of expert opinions. In: Nunamaker JF, editor. Proceedings of the Annual Hawaii International Conference on Systems Sciences HICSS-32, 1999; Maui, HI, USA. New York: IEEE Press.
[33] Rutscher A, Salzsieder E, Fischer U. KADIS: model-aided education in type I diabetes, Karlsburg diabetes management system. Comput Methods Programs Biomed 1994;41(3/4):205–15.
[34] Serrano-Rios M, Lefebvre PJ. Diabetes 1985. Amsterdam, The Netherlands: Excerpta Medica; 1986.
[35] Weiss G. Multiagent systems: a modern approach to distributed artificial intelligence. Cambridge, MA: MIT Press; 1999.
[36] West BJ. Fractal physiology and chaos in medicine. Teaneck, NJ, USA: World Scientific; 1990.
[37] Wooldridge M, Jennings NR. Intelligent agents: theory and practice. Knowledge Eng Rev 1995;10(2): 115–52.