A Virtual Patient Based on Qualitative Simulation

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ABSTRACT

In this paper, we describe the development of a virtual human to be used for training applications in the field of cardiac emergencies. The system integrates AI techniques for simulating medical conditions (shock states) with a realistic visual simulation of the patient in a 3D environment representing an ER roomIt uses qualitative simulation of the cardio-vascular system to generate clinical syndromes and simulate the consequences of the trainee's therapeutic interventions. The use of knowledge-based simulation provides a strong basis to integrate the behavioural aspects with the graphical appearance of the patient in the virtual ER. This also supports the creation of an emotional atmosphere increasing the realism of the training system.

Categories and Subject Descriptors

J.3 [**Life and Medical Sciences**]: Medical Info Systems.

General Terms: Human Factors, Design.

Keywords: Virtual Humans, Qualitative Simulation, Interface Agents, Emotional Interfaces, Artificial Intelligence in Medicine.

1. INTRODUCTION

Virtual humans are an important component of intelligent user interfaces. They can serve as intelligent assistants or instructors [16] or be part of complex simulations, where they play an important role for realism and, in critical training applications, a sense of emotional involvement [18]. In medical applications, Virtual humans would constitute natural interfaces to knowledge-based systems, as virtual patients displaying the symptoms associated with a given pathology. Yet, little work has been dedicated to the integration of knowledge-based systems into 3D virtual patients. In this paper, we describe the development of a virtual patient for a specific area of medicine, cardiac emergencies.

In addition, since this system is targeted at training medical students in emergency decision-making, this is a rationale to try to convey emotional aspects as well, in this highly specific context. In the next sections, after giving an overview of the system, we describe the AI technique used to simulate the patient condition, which is derived from qualitative simulation [19]. We show how qualitative simulation can serve as a central principle for the integration of the various components of the interface.

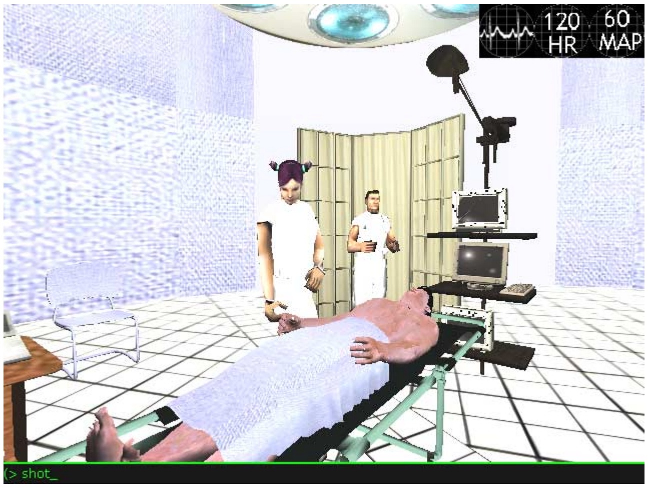

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Figure 1. System Overview.

2. RELATION TO PREVIOUS WORK

Virtual Humans have been extensively described in virtual reality surgery but little work has been dedicated to them in other areas of medicine, in particular clinical medicine, which requires physiological rather than just anatomical modelling. While 2D virtual patients have been used as interfaces to computer-aided instruction systems [8] only Badler et al. [2] [6] [7] have described the use of an autonomous 3D virtual human to simulate battlefield casualties in military simulations. Their virtual human displays symptoms corresponding to the injuries suffered on the battlefield, while the trainee medic controlled by the user would attempt emergency treatment.

However, there exist several important differences with our application.

We use physiological models as an "internal" model of the patient itself. This contrasts with the modelling of pathologies themselves through PaTNets, which is more in line with causal networks in medicine, and provide a model of the evolution of the pathology, rather than an internal model of the patient. PaTNets are behavioural representations based on transition networks that can represent transition between states, and as such can be used to model the evolution of a clinical situation. For instance a PaTNet for a tension pneumotharax directly associates causes to symptoms and stores variables evolutions for treatment [6]. Using a physiological model provides a stronger integration at various levels of the system and better prospects for knowledge representation. In addition, the same

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principles can be used to represent both normal and pathological cardiac function.

Further, the patient's visual appearance can be mapped to its internal model. Treatment can operate on the original model, rather than having a dedicated PaTNet or representation. Of course, this is facilitated in our application by the fact that pathophysiological models are easier to derive in clinical medicine (especially in cardiology).

Finally, we adopted a first-person, rather than third person, viewpoint. This creates a stronger user involvement and emphasises emotional aspects (creating a setting more similar to [18] than to [3]).

3. SYSTEM OVERVIEW

The system presents itself as a 3D environment featuring the virtual patient in an emergency room. Figure 1 gives an overview of the interface from the user's perspective. The user can thus see the virtual patient, whose appearance varies according to its clinical condition, as well as monitor vital parameters such as Heart Rate (HR) and Mean Arterial Pressure (MAP). Other parameters are only accessible through specific complementary examinations (for instance, Pulmonary capillary pressure, PCap, via cardiac catheterisation), which have to be requested by the user.

In addition to the patient, the environment is populated with other autonomous agents representing ER nurses. These serve as interface agents, executing users requests for diagnosis and treatment. The trainees' instructions are transmitted to the nurse using speech recognition (in Japanese), based on a simple command language describing the potential actions and their parameters, such as the injection of a given drug.

In the first instance, the system generates a clinical condition for the virtual patient. For instance, a cardiogenic shock will be simulated by altering variables such as inotropism (cardiac contractility), and to some extent other associated variables, such as those dealing with cardiac relaxation. From this initial alteration, the system propagates the consequences of the primary dysfunction by simulating various cycles of cardiac processes until a steady state is reached. The simulation of the patient generates values for all physiological parameters and, as a result, provides the trainee with the relevant set of clinical symptoms.

In the virtual ER room, the trainee can carry out complementary examinations that will assist diagnosis. Finally, s/he will choose a treatment to be administered to the patient; the same mechanisms will then simulate the impact of treatment and result in a new clinical appearance for the patient.

In the next sections, we describe the qualitative simulation method used to simulate the cardio-vascular system and how this approach facilitates the visual integration of the interface. We then comment a detailed example from a fully implemented prototype of the system.

3.1 System Architecture

The system architecture (Figure 3) is developed using a state-of-the-art 3D game engine, Unreal Tournament™ with the incorporated Warfare engine, as a development environment [14]. The engine supports high quality graphics, as well as the animation of virtual characters, used for the patient and the nurses. Besides, it includes an excellent development environment that supports the authoring of animations for virtual humans behaviour, as well as various mechanisms (dynamic link libraries and socket-based inter-process communication) for integrating external software, such as the cardiac simulation module and the speech recognition system. Our software architecture is based on UDP socket communication between the 3D graphics engine and the qualitative simulation module, which has been developed in Allegro Common Lisp™.

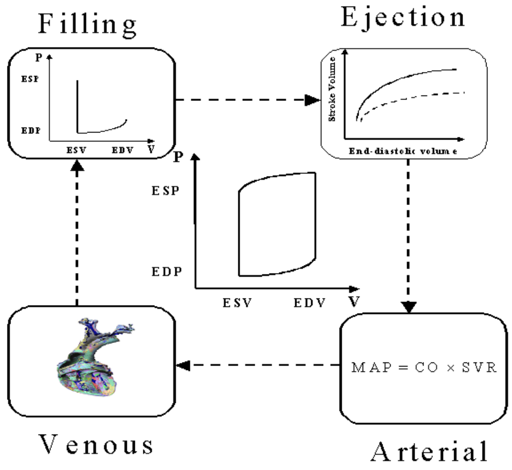

Figure 2. Modelling the Cardiac Cycle with Qualitative Processes (see text). EDV: End-Diastolic Volume; EDP: End-Diastolic Pressure.

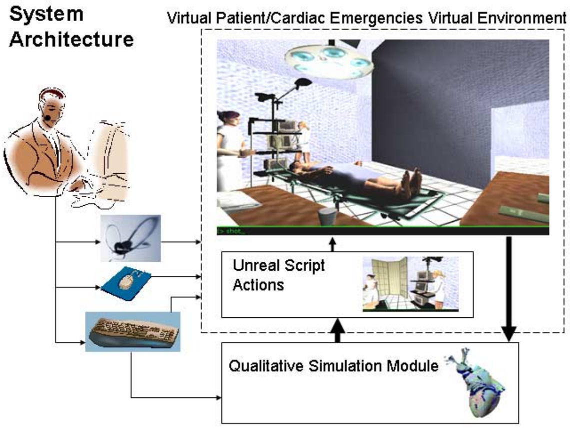

Figure 3. System Architecture.

Formatted UDP messages transmit selected physiological parameters to the graphic environment: those that are visible through the monitors and those that impact on the patient's appearance and behaviour. These parameters are for instance Mean Arterial Pressure (MAP), Heart Rate (HR), Systemic Vascular Resistance (SVR), and Pulmonary Capillary Pressure (PCap).

In the next section, we describe the use of qualitative processes to implement the patient's physiological model. In particular, we show its potential for providing an integrated solution, which plays a major role when embedding the behavioural engine within a graphical and interactive simulation.

4. QUALITATIVE SIMULATION OF THE CARDIO-VASCULAR SYSTEM

Qualitative simulation aims at modelling the behaviour of the cardio-vascular system, both in normal and pathological circumstances. Cardiac dysfunctions are simulated using the same model, but with different initial conditions.

Qualitative simulation has been essentially developed for physical systems and mechanical devices [19] and is best known through work in qualitative physics.The main idea consists in reasoning on physical phenomena by abstracting physical descriptions. Yet, the same techniques have been used to model physiological systems: for instance, the QSIM approach [12] has been applied to the cardio-vascular system by Kuipers as early as 1985 [13].

The rationale for the use of a qualitative approach in physiology is that numerical simulations of the cardio-vascular systems are faced with many limitations: it is sometimes difficult to observe convergence of the set of equations that govern the system, manifesting a difficulty to integrate a large set of experimental equations obtained on sub-systems. More importantly, numerical models often behave as black boxes, which make them difficult to interface with other software modules.

Another source of development of qualitative models in physiology has been the search for deep knowledge representations in medical knowledge-based systems [17] [4]. These were developed to generate clinical situations from first principles, simplifying the implementation and maintenance of medical knowledge-based systems.

Cardiology, especially blood pressure regulation, has been a major area of application for qualitative modelling: Long [15] formalised cardiac physiology using a causal network, and Kuipers adopted his QSIM approach to cardiac dynamics [13]. In his application, he used the equations for cardiac output and blood pressure such as:

$$\text{Cardiac Output} = \text{Heart Rate} \times \text{Stroke Volume} \quad (1)$$

$$\text{Mean Arterial Pressure} = \text{Cardiac Output} \times \text{Systemic Vascular Resistance} \quad (2)$$

to create a constraint network, through which variables' changes are propagated until a complete new state is generated. In Kuipers' approach, the influence of parameters not part of equations was represented using the M+ operator (representing a monotonic function, for instance to represent the influence of inotropsim on stroke volume). However, physiological equations, unlike physical laws, do not map directly onto the observed phenomena, hence they do not represent accurately the behaviour of the cardiovascular system (let alone the causal implications). In particular, it is difficult to relate the time course of variable updating to the actual dynamics of the cardio-vascular system. Like with causal networks, the dynamics of constraint propagation might not always reflect the actual system dynamics. Temporal probability models have been used to represent the dynamics of some pathological situations (cardiac arrest, [11]), but these do not qualify as "deep models" in the sense described above.

Widman [20] proposed another qualitative model of the circulatory system, using a more sophisticated description that emphasised structure/function relationships. In his model, the function of each component of the cardio-vascular system is explicitly identified and causal relations are established between the various functions. For instance, cardiac ventricles are associated in this model to filling and ejection functions in the cardiac contraction cycle.

Since we're using a virtual human as an integrated interface to the simulation system, the latter should underlie a natural mapping between internal processes and the physical appearance of the virtual patient.

In the next section, we describe the representations used for qualitative simulation technique used and how they support integration with the visual aspects of the interface.

4.1 Qualitative Processes in Cardio-circulatory Physiology

Forbus has introduced Qualitative Process Theory (QPT) [9], which is centred on the identification of physical processes, within which the causal influence between variables is encapsulated. This approach is much closer to the description of physical phenomena themselves.

QPT has been successful in modelling complex mechanical devices. It has a real potential for modelling physiological systems as well. Due to the complexity of physiological systems, it is most difficult to derive a consistent set of confluence equations for such systems, which makes other qualitative approaches difficult to use. Besides, it is also necessary to capture a certain ordering of some physiological processes, such as the ones that correspond to the cardiac cycle.

Because physiological knowledge tends to be expressed through processes encapsulating physiological laws [1], the use of a process-based representation facilitates knowledge elicitation. The same model accounts for normal and pathological conditions: the latter corresponding to steady-states reached after alterations to normal values of physiological parameters.

The medical knowledge underlying the simulation of circulatory shock states is naturally formalised as physiopathological schemata in intensive care textbooks [1]. The knowledge has been encoded from textbooks' descriptions under the supervision of specialised physicians who also participated in the testing of the first prototype (which at this stage was limited to the validation of results obtained for shock states and their treatment). The development of this prototype has also been done in co-operation with consultants from the University of Gifu's School of Medicine.

For instance, Frank-Starling's law describes the relation between ventricular ejection and "pre-load" (the level of ventricular filling prior to contraction), this relation depending on cardiac contractility (inotropism) as well. Causal networks relating the three determinants of cardiac function (contractility, pre-load, afterload) fail to capture the inter-relations between the various determinants [5]. On the other hand, complex inter-relations can be captured in a process-based representation.

The qualitative influence relations are derived from the shape of the curve of Frank-Starling's law, and they are used to propagate variable changes as part of the qualitative simulation cycle (which is actually similar to a Pressure-Volume curve in thermodynamics). The qualitative translation gives two levels of influence depending on the segment of the curve. This can be represented by maintaining two separate influence equations for each segment of the Frank-Starling curve, the influence equation to be used being determined by a threshold value of the pre-load. The threshold value itself depending on inotropism, this representation is able to integrate all influences. Qualitative influence relations can be representing by adapting the influence relations of QPT: the positive influence of inotropism on Stroke Volume will be formulated as: I+(inotropism, SV). These equations are implemented as linear relations between qualitative values, in some cases within pre-defined intervals.

Four main processes account for the circulatory dynamics: venous return, ventricular filling, ventricular contraction and arterial system behaviour (Figure 2). The central "P-V" curve on Figure 2 represents the cardiac contraction cycle. Ejection and Filling Processes can be represented as segments of this curve, from which linear influence relations can be derived between qualitative variables.

Two of these processes represent cardiac function and the two others the behaviour of the arterial and venous system, not unlike Widman's model [20].

At each sub-level, we have identified key physiological processes, and described relations between qualitative variables involved in these processes, though influence equations inspired from QPT. One variant is that we work on orders of magnitude of parameter variation rather than with their absolute values. Each of these processes involves a sequence of sub-processes. For instance, ventricular contraction involves sub-processes for ejection, Frank-Starling's law and the effects of after-load (Figure 4).

Influences can be embedded in the description of processes. For instance, the effect of cardiac frequency on ventricular filling (ventricular filling decreases when cardiac frequency is high) can be included in one of its sub-processes.

Processes can also represent compensatory mechanisms (such as baroreceptors), which are triggered under specific circumstances and play a role in the short-term regulation of arterial pressure. We have described a total of 25 sub-processes, including regulatory mechanisms. A typical process involves between 3 and 7 physiological parameters, taking into account that in some cases both the parameter value and its variation can be required. In addition, embedded procedures are computing key values such as cardiac output and MAP using equations such as (1) and (2). However, unlike in [13] these equations are not used as causal representations.

```
{MainProcess Ejection

 [Process Frank-Starling
   ...
   I++(Contractility (I+(TeleDiastolicVolume, SV))]

 [Process Contractility
   ...
   I+(Contractility, SV)]

 [Process Afterload
   ...
   I-(Afterload, SV)]

 [Process Cardiac-Pump
   ...
   I-(SV, TeleSystolicVolume)] }
```

Figure 4. Pseudo-code for Qualitative Processes, showing the Qualitative Influence Relations.

Temporal aspects are also easier to represent in a process-based approach than with confluence or constraint equations. For instance, if we consider the example of a blood loss, the first process affected is venous return, which impacts on ventricular filling, then ejection and finally the arterial system, causing a fall in MAP and triggering short-term mechanisms for maintaining arterial pressure (baroreceptors).

The various processes are activated as a cycle, which reproduces the cardiac contraction cycle. Each process is attached a set of methods corresponding to the influence part of qualitative process theory. The post-conditions of some processes behave as the pre-conditions of the next process: in other-words, some processes create parameter variations that act as an input for subsequent processes. For instance, cardiac contraction sets the value of the stroke volume, which is a determinant of arterial pressure in the arterial system process, etc. Hence the updating of variables and propagation of influences does follow the structural and temporal cycle of the cardio-circulatory system.

5. GRAPHICS AND ANIMATION: THE INTERFACE

The graphic presentation of the interface aims at recreating a realistic environment, which is displayed in a first-person view to the user, for maximum involvement. The system supports different forms of user interaction. The user is allowed to navigate in the virtual environment to observe the patient from various angles (this might be required to observe breathing patterns for instance): it also forces the trainee to actively observe symptoms without having to exaggerate these.

The interface constantly displays vital parameters (HR and MAP) through the usual monitoring devices. Additional investigations can be carried out by instructing nurses: for instance, the user can ask for a reading of pulmonary capillary pressure, or enquire about the patient's diuresis (another parameter whose value qualifies the shock state). The same mechanism applies for selecting a drug therapy. All instructions to the nurses can be issued via an interface menu or, more realistically, by using a speech recognition system (in Japanese).

5.1 Mapping Simulation Parameters to VH Animation

As the qualitative simulation system corresponds to the virtual patient's physiology, this facilitates the mapping between the simulation's results and the patient's appearance. The effect of therapeutic drugs can also be translated directly in terms of the physiological parameters targeted by these drugs (for instance, inotropism for beta-agonists).

The system uses Unreal's dynamic textures to create a realistic appearance: these textures have been edited from real photographs obtained from medical teaching material. For instance, when a shock state appears, the texture will be shifted to pale, sweaty skin for the face. The face texture is under control of MAP mainly, while limb textures are selected using both MAP and SVR parameters.

It is also possible to trigger animations (or modify the "idle animations" of the virtual human) as a function of the overall gravity of the patient's condition (for instance, using the actual level of CO/MAP to qualify the gravity of the shock state). For associated symptoms, such as dyspnea associated with pulmonary edema, a specific animation can be triggered whenever PCap goes beyond a given threshold, modifying the frequency and amplitude of breathing movements in the patient's animation. Figure 5 shows various patient's appearances:normal appearance (left), cyanosis (right).

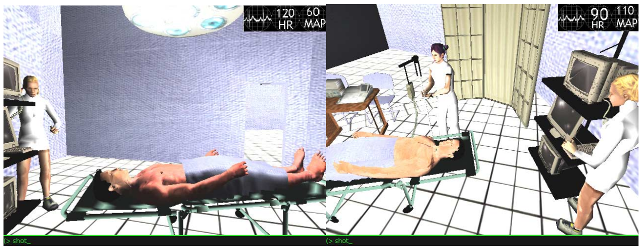

Figure 5. Patient's appearance in pathological and normal states.

5.2 Emotional Aspects of the Interface

A realistic simulation should render the atmosphere and tension created by the critical nature of the situation. There are several factors that contribute to emotional communication in such a situated context.

The first one is the overall visual realism of the environment, including its complexity, appearance, lightning, multiple actions and disturbances, background sounds and noises. This recreates the original atmosphere and, unlike some traditional training systems, sometimes requires active exploration of the environment from the trainee to acquire information (for instance, a monitor may not be visible from a given perspective).

The character's appearance is the most direct manifestation of the gravity of the situation. In addition to the clinical signs of gravity (e.g. cyanosis or dyspnea, described above), we have implemented behavioural scripts governing spontaneous movements and reactivity (indicating e.g. loss of consciousness, pain, etc.). The latter elements are loosely connected with diagnosis, but play an important role in creating emotional tension and a sense of gravity.

The third one is constituted by the additional characters, in this case the nurses. They can be used to give non-verbal feedback on the situation and on the users decisions, or lack of decisions. This can take place as non verbal behaviour, but is mostly reflected through situated behaviour, i.e., the manner in which the nurses will react to the user or carry out their activities.This is implemented by using parameterised models of such activities, tuned in real-time to the gravity of the overall situation. In addition, various scripts can be triggered when the patient's situation deteriorates or fails to improve following the user's choice of therapeutics.

This approach also follows recent work showing how virtual characters' attitudes could convey emotional content [10].

6. AN INTEGRATED EXAMPLE

A first prototype of the system, integrating all the above features, has been fully implemented. In this section, we describe into more detail a running example from the system, which shows the level of integration achieved between the graphics and the qualitative simulation.

6.1 Initial Conditions and Simulation

This example is a simulation of cardiogenic shock.Cardiogenic shock can be simulated by primitively decreasing the value of the inotropism parameter, which corresponds to the quality of cardiac contraction. The system works by simulating events through the cardiac cycle, the various physiological processes being ordered according to this cycle. Several simulation cycles are taking place until the qualitative values reach a steady-state. The first event simulated is cardiac contraction. The main output variable for this process is the Stroke Volume (SV; the amount of blood ejected by the heart at each contraction), from which it is possible to compute cardiac output and mean arterial pressure. Three sub-processes are active for the three main determinants of cardiac contraction. These incorporate influence equations that can be expressed in the classical framework of Qualitative Process Theory: I+(Pre-load, SV), I+(Inotropism, SV), I-(Afterload, SV).

The influence relation, I+, is actually modelled by abstracting the shape of the corresponding physiological curve. For instance, in the case of Frank-Starling's law, rather than just using a "linear" influence model, the influence is strong for low values and exhibits a saturation effect for higher ones.

But actually Frank-Starling's law depends itself on the level of Inotropism, and the influence of pre-load on stroke volume is more significant for higher inotropic states. If a "second-order" notation was allowed for influence equations, these could be formulated as: I++(Inotropism, (I+(Pre-load, SV))). In terms of the actual implementation, the level of inotropism shifts the coefficients of the I+(Pre-load, SV) qualitative relation upwards.

The primitive decrease in Inotropism causes a decrease in SV of the same order of magnitude: a "--" value for Inotropism would lead to a similar value for SV.

The next process consists in the arterial system: this is where parameters such as CO and MAP are computed, by using the corresponding physiological equations (see equation 1). Here these equations are used with the qualitative values. However, they correspond to simple computations in our approach. Unlike Kuipers [12], we are not using the equations to represent any causal mechanism, which is modelled through the processes themselves. This leads to qualitative values of "---" for CO and MAP. In the first simulation cycle, the baseline HR and SVR values are used.

Mechanisms for the short-term regulation of arterial pressure (such as baroreceptors and chemoreceptors) are represented as sub-processes of the Arterial System. Here the baroreceptor process reacts to a fall of MAP to trigger an increase in HR, SVR and Venous Tone (VT): I+((d-MAP < 0), HR) ; I+((d-MAP < 0), SVR) ; I+((d-MAP < 0), VT). This notation means that "conditional" influence equations are triggered for negative variations of MAP (d-MAP < 0). As a result the new qualitative values for HR are "++" and SVR are "++". These are implemented by methods encapsulated in the process representations.

The next process is the Venous System, which includes several processes including venous return. The most important influence here is that increased VT increases ventricular venous return.

The last process of the cycle is cardiac filling. This is simplified in our model, which is mostly a Left Ventricle model, where the role of the right ventricle is a coarser model (not modelling specifically right ventricle contraction and pulmonary circulation). In this process, ventricular filling is increased by increased venous return: I+(VT, preload).

The second cycle of simulation activates again the cardiac contraction process under the new conditions that result from short-term adaptive mechanisms. The increase in preload fails in improving the stroke volume I+(preload, SV), as this process depends on the levels of inotropism, which is primitively decreased. Hence the qualitative value of SV remains low "---".Then the Arterial System process is triggered again, and the calculations take into account the updated HR and SVR values (as modified by the compensatory mechanisms). The increase in SVR fails to restore

MAP for severe alterations of inotropism, just like the increase in HR fails to restore CO (we're not considering in this example the negative impact of high HR on left ventricular filling and oxygen consumption by the heart).

The full set of physiological parameters is not visible to the trainee at this stage, to reflect the difference between the physiological parameters that have a clinical translation, those which can be measured by complementary investigations (such as Pulmonary capillary pressure or Cardiac Output) and those inaccessible to examination, but that can be part of a pathophysiological *a posteriori* explanation.

The system maps those physiological parameters that have a clinical translation to the virtual patient's appearance. Peripheral vasoconstriction will result in pallor and cold extremities, etc., while prolonged or severe shock state could also result in cyanosis. Depending on the severity of global cardiac dysfunction and the corresponding central venous pressure, jugular veins might become enlarged on the patient.

This state can be difficult to distinguish from other causes of shock on observation alone, which is precisely the purpose of such a training system. Figure 6 shows the specific patient appearance for cardiogenic shock.

6.2 Choice of Therapeutics and Further Simulation

Once the simulation has reached a steady state, one of the nurses will prompt the trainee to order a treatment. The system is actually developed as a realistic simulation, in which the user has to directly treat the patient and observe the consequences, rather than a traditional instructional system in which s/he would be first asked for a diagnosis. The user has a choice between eight major (medical) therapeutics, some of which can be given in association. A dosage can also be associated to the therapeutic chosen; for instance, fluid expansion can be conservative or more aggressive, or beta agonists (such as dobutamine) can be given in various dosages.

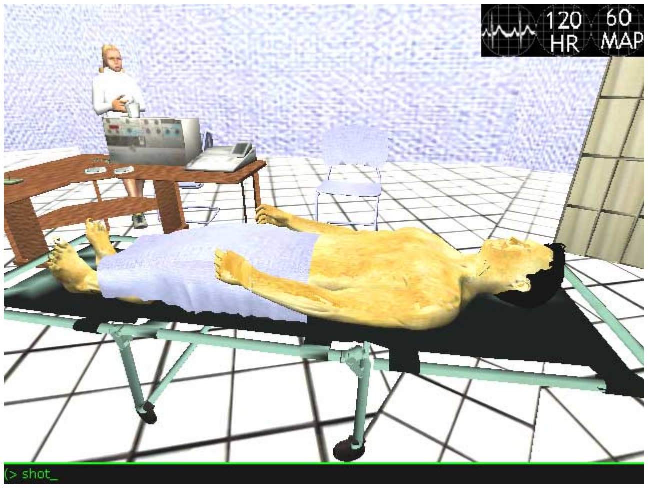

Figure 6. Cardiogenic shock.

As we have seen, the effects of therapeutic drugs are simulated by modifying the physiological parameters that are targets for the drugs actions: for instance, beta-agonists will increase inotropism (with a side effect of increasing heart rate as well) and fluid expansion directly increases blood volume. This mechanism is similar to the one used for generating the clinical syndrome, and is realistic from a physiological standpoint.

In the above cardiac shock example, we have selected two courses of action depending on whether the user chooses a correct or a wrong treatment.

Faced with primitive cardiac failure (whatever its aetiology) the appropriate pharmacological treatment at the acute phase consists in administering beta-agonists (such as dobutamine), which restore inotropism. The qualitative simulation module, starting from the current status (and corresponding values of physiological parameters) simulates another set of cardiac cycles with an increased value for inotropism. This will improve the cardiac contraction process, raising cardiac output and restoring MAP to a still low, but less life-threatening value. As part of its side effects, the drug maintains an increased heart rate. In turn, the patient's appearance is also modified to reflect the improvement.

If failure of the cardiac pump is the main cause of shock, increasing blood volume by fluid expansion will not restore arterial pressure; even worse, it would cause a fluid overload leading to a life-threatening pulmonary edema. When the PCap raises below a certain threshold this tends to cause pulmonary edema (i.e. lungs alveoli are filled with water, preventing normal pulmonary function). In the absence of an accurate modelling of the respiratory system, the patient's breathing pattern is directly altered when PCap raises above a threshold, and corresponding animations are triggered. Needless to say, breathing rhythm is a powerful indicator in the creation of an emotional tension, though this has not been much explored in non-verbal behaviour.

The choice of the wrong therapeutics together with the possible aggravation of the patient status wills also adverse behaviour from the nurse (Figure 7).

Figure 7. Emotional Reactions.

7. CONCLUSIONS

We have described the development of a virtual patient for clinical medicine, which could constitute an ideal interface for many knowledge-based systems in Medicine. The need to generate clinical situations from first principles, which justifies the development of physiological models, also provides more realistic models that are easier to interface with the appearance and behaviour of virtual humans. In this context, the development of a virtual patient can be seen as an integration of a visual model and a physiological model, which is also a realistic model of the "internal behaviour" of the patient. As a result, a higher level of integration can be achieved with this approach than in systems in which the virtual human is mainly an interface to traditional knowledge-based systems. Further developments will extend the cardiovascular model to incorporate myocardial perfusion, and the interplay between cardiac and respiratory physiology.

8. ACKNOWLEDGMENTS

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