Qualitative Physiology: from Qualitative Processes to Virtual Patients[1]

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Abstract

In this paper, we describe an implementation of qualitative physiology in the field of cardiac emergencies, which is integrated to a 3D virtual patient. . The system integrates qualitative simulation techniques with a realistic visual simulation of the patient in a 3D environment representing an ER room. We have adapted Qualitative Process Theory (QPT) to the representation of physiological processes in order to be able to generate appropriate pathophysiological models. After a brief review of the use of qualitative simulation in cardiology, we describe how a subset of cardiac physiology can be modelled using qualitative process theory and discuss knowledge representation issues. We then present results obtained by the system and the benefits that can be derived from the use of a virtual patient in terms of training. Finally, we explore the problem of integrating multiple pathophysiological models for various aetiologies of shock states.

Introduction

The methods of qualitative physics have been applied to physiological systems since the early days of qualitative physics in the 80s [6] [8] [9]. In this paper, we describe the use of qualitative process theory to model physiological processes of the cardio-circulatory systems.

This is part of an attempt at developing virtual patients in clinical Medicine. While there exists substantial amount of research aiming at developing virtual patients for surgery, very little work has been dedicated so far to the use of virtual patients in clinical medicine. The main work on 3D virtual patients outside virtual surgery has been that of Badler et al. [2] who have described the use of an autonomous virtual human to simulate battlefield casualties in military simulations, still in the field of trauma rather than clinical medicine.

The paper is organised as follows. After a brief reminder of the use of qualitative simulation in cardiology and an overview of our system architecture, we describe our own implementation and discuss knowledge representation issues. We then present an extended example from the system, including the visualisation of symptoms on the virtual patient. We conclude by discussing the integration of multi-system models around this qualitative model, in order to achieve more complex simulations.

Qualitative Simulation in Physiology

Cardiology, especially blood pressure regulation, has been a major area of application for qualitative modelling, probably because of the abundance of pathophysiological descriptions and their relevance to diagnosis and treatment. It can thus be noted that, from confluence equations [4] to the QSIM approach [6], most of qualitative simulation theories have been adapted to cardiac physiology.

Our own approach [3] revisits qualitative process theory [5] applying it to the cardio-vascular system.

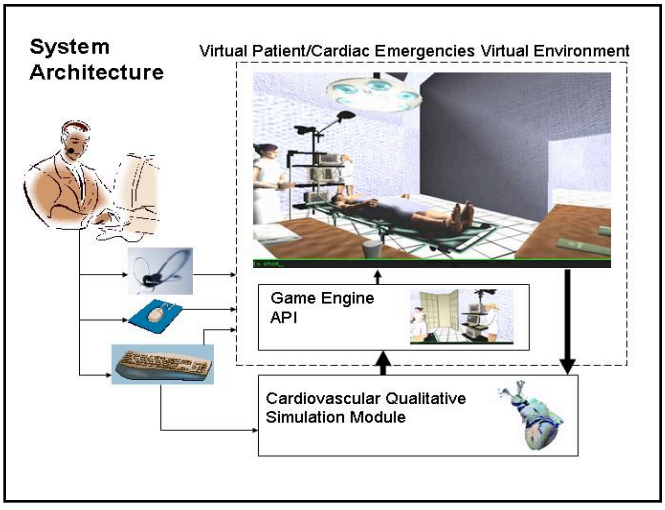

Figure 1. System Architecture

[1]An extended version of this paper will appear in the proceedings of the AIME (Artificial Intelligence in Medicine Europe) 2003 Conference.

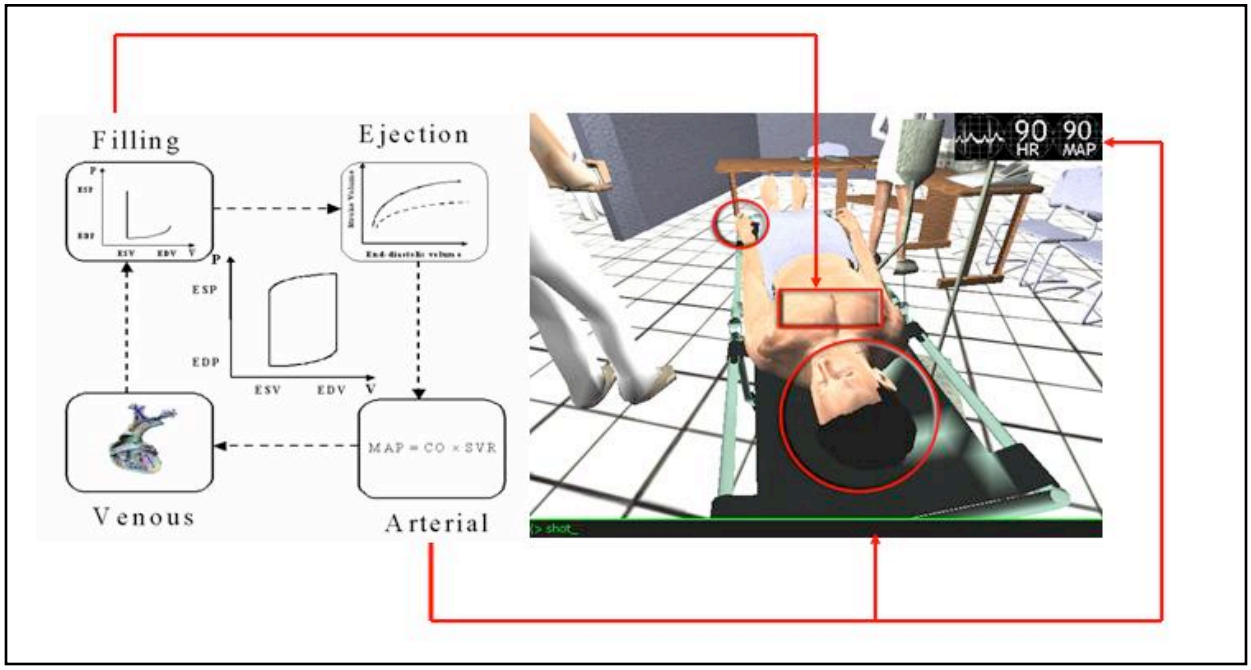

Figure 2. Physiological Processes and Parameter Mapping to Patients' Status

System Overview and Architecture

Our system integrates a qualitative simulation module within a 3D virtual patient (Figure 1). The visualisation component is based on a state-of-the-art 3D game engine, Unreal Tournament 2003™ [7].

It supports high quality graphics, as well as the animation of virtual characters, used for the patient. Besides, it incorporates a sophisticated development environment that supports the authoring of animations for virtual humans behaviour, as well as multiple mechanisms (dynamic link libraries and socket-based inter-process communication) for integrating external software, such as the qualitative simulation module.

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™. The system generates a complete pathophysiological simulation from initial alterations corresponding to the pathological situation to be simulated (for instance, by primitively decreasing inotropism). The set of parameters obtained is interpreted and displayed as clinical signs (e.g. pallor, enlarged jugular veins, etc.) or as data on the monitoring devices (HR, MAP).

All these visual elements can be updated throughout the simulation to reflect a deterioration or an improvement of the patient's situation. The visual appearance of the patient is based on dynamic textures that can reflect a relevant range of shock situations (pallor, "warm shock", cyanosis, etc.).

Implementing Qualitative Processes in Cardiac Physiology

Qualitative Process Theory (QPT) [5] was introduced by Forbus as one of the main techniques of Qualitative Simulation.

It is centred on the identification of physical processes, within which the causal influence between qualitative variables is encapsulated.

QPT has been successful in modelling complex mechanical devices and 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 or QSIM-like) equations for them, which make other qualitative approaches more difficult to use, especially with the prospect of integrating multiple organ systems in the long term. Because physiological knowledge tends to be expressed through processes encapsulating physiological laws [1], the use of a process-based representation also facilitates knowledge elicitation. We have defined some 24 processes corresponding to various physiological mechanisms, such as the determinants of ventricular filling

(e.g., ventricular venous return, relaxation and passive elastance) or ventricular ejection (effects of inotropism, preload, afterload, etc.) as well as various compensatory mechanisms (e.g. baroreceptors). These processes are encapsulated into four macro-processes: ventricular filling, ventricular ejection, arterial system behaviour, venous system behaviour.

These macro-processes have both structural and functional interpretations: they correspond to the main compartments of the circulatory system, within are associated key physiological functions. In the course of the simulation, these four macro-processes are activated in turn, in a way that reflects the cardiac cycle (the "P-V" curve on Figure 2 represents the cardiac contraction cycle).

The variables we defined are directly adapted from actual qualitative variables used in the description of cardio-circulatory pathophysiology. Hence they can take any of nine values, from " ↓ ↓ ↓ ↓ " to " ↑ ↑ ↑ ↑ " . The fact that in physiology textbooks and literature, qualitative variables such as and +/- are used indifferently means that the values considered do not distinguish between variation and final value, as they are interested to steady states for the timescale considered. Influence equations formalise the relations between variables in terms of their variation. For instance an influence equation such as I+(inotropism, SV) indicates that stroke volume increases with inotropism, while I-(afterload, SV) that it decreases when afterload increases. Influence equations are generally assumed to be linear considering that they apply to a small set of qualitative values. However, we had to adapt the traditional notion of influence equation to the context of physiological laws, where influences are more complex.

One such example is Frank-Starling's law, which describes the relation between ventricular ejection (rep-resented by the stroke volume) and "pre-load" (the level of ventricular filling prior to contraction, corresponding to the End-Diastolic Volume), this relation depending on cardiac contractility (inotropism) as well.

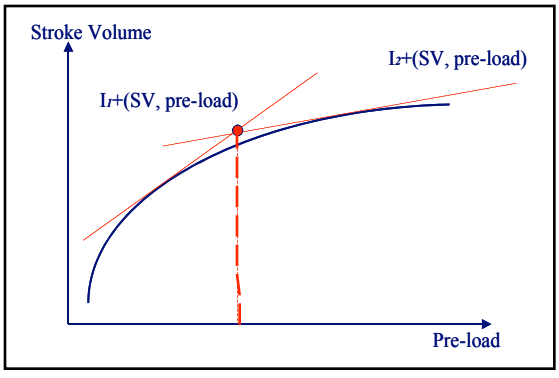

Figure 3a. Converting Starling's Law into Influence Equations.

This can be represented by maintaining two separate influence equations for each segment of the Frank-Starling curve (Figure 3a), the influence equation to be used being determined by a threshold value of the pre-load. I1+(preload, SV) and I2+(preload, SV), which have different influence coefficients of the influence coefficient, _, is explicitly represented in the equations of Figure 3b, in which pre-load is actually represented by End-Diastolic Volume (EDV)).

The transition point between these two influence equations, i.e. the preload value for which the increase of SV is less significant is dynamically computed at each cycle as a function of the inotropic state (Figure 3b).

[Process *Frank-Starling*

I+(Ino, EDV*lim*)

if EDV > EDV*lim*
□ = □1 else □ = □2

I+(□, (EDV, □-SV))]

Figure 3b. Part of the QP formalisation for Starling's Law.

We have defined three different kinds of processes (though they are formalised in an uniform fashion): Physiological Laws, Regulatory Mechanisms and Computational Processes.

Physiological laws describe the basic principles governing a given organ's function: they are often ex-pressed as relations between variables or concepts, with a strong element of causality. Their formulation very often reflects the way the laws have been established empirically and several laws tend to be de-scribed for related phenomena (which explain their sometimes complex graphical representations resorting to a family of curves).

Regulatory mechanisms are physiological behaviours that are triggered in response to a physiological status to restore the value of parameters. For instance, baroreceptors trigger an adrenergic response, in-creasing Hear Rate and Systemic Vascular Resistance whenever arterial pressure drops suddenly.

Computational Processes simply compute values of parameters that take part in physiological equations, such as those governing Cardiac Output and Mean Arterial Pressure.

Overall, our model includes 28 primitive parameters, which account for the main physiological variables: Stroke

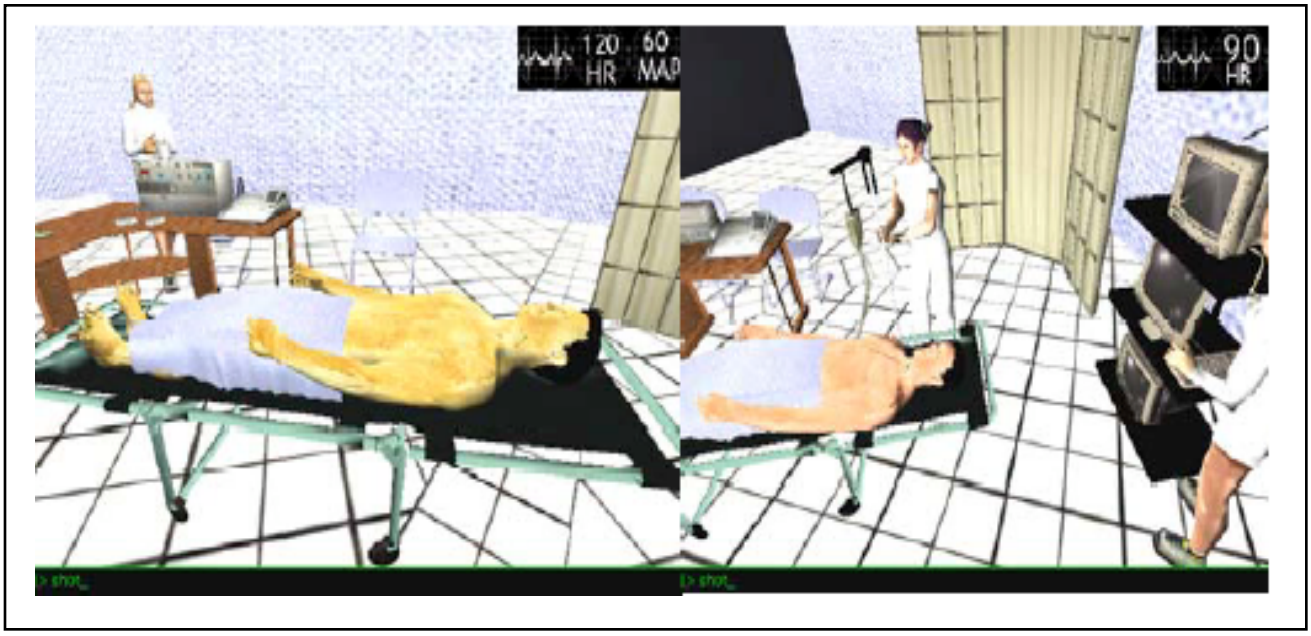

Figure 4. Treatment of Cardiogenic Shock

Volume, End-Systolic pressure and volume, End-Diastolic pressure and volume, systemic vascular resistance, inotropism, etc. A typical process operates on several parameters (3 to 6) and contains a corresponding number of influence equations.

Results

The initial validation procedure involved the generation of the main shock syndromes by altering corresponding primitive variables: inotropism for cardiogenic shock, SVR and arterial properties for anaphylactic and toxic shocks, blood volume for haemorrhagic/hypovolemic shock. The results provided by the system in terms of the main physiological parameters (MAP, HR, CO, SV, EDV, EDP, etc.) are consistent with the traditional description of these syndromes in the literature, though they are all generated through a complex cycle of simulation. In addition to the main shock syndromes, the system is able to simulate a range of cases of short-term adaptation of the cardiovascular system.

We give a detailed example of the simulation of a cardiogenic shock. The simulation of cardiogenic shock is triggered by primitively decreasing the value of the inotropism parameter, which corresponds to the intensity of cardiac contraction.

The qualitative simulation procedure reflects the integrated events of the cardiac cycle. This means that each macro-process (Ejection, Arterial System, Venous System, Ventricular Filling, see Figure 2.) are activated in turn, until a steady state is reached, represented by the stability of the qualitative variables describing the system. In the following example, we describe events within each macro-process without detailing them in terms of sub-processes (we only mention relevant influence equations encapsulated within these sub-processes):

Ejection Process

The primitive decrease in inotropism is responsible for a decrease in Stroke Volume through influence equation I+(Inotropism, SV), and an increase in the residual volume (ESV, End Systolic Volume ↑ ↑).
Variables: (Inotropism ↓ ↓ ↓, SV ↓ ↓ ↓, ESV ↑ ↑).

Arterial System

New values are computed for CO and MAP. Baroreceptors are triggered by the fall in MAP and result in increased HR, increased Systemic Vascular Resistance and Venous Tone. Variables: (CO ↓ ↓ ↓, MAP ↓ ↓ ↓, HR ↑ ↑, SVR ↑ ↑).

Venous Return

Increased venous tone yields an increase in ventricular venous return. Variables: (VT ↑ ↑, VVR ↑ ↑).

Ventricular Filling

Ventricular filling is increased by the additional venous

return due to increased venous tone: I+(VT, preload) and the augmented residual volume ESV. Variables: (EDV ↑ ↑, EDP ↑ ↑).

Ejection Process (new cycle)

The increase in preload fails in improving the stroke volume significantly as the influence I+(preload, SV) depends on the levels of inotropism, which is primitively decreased. Nor is the increase in HR sufficient to increase CO. Variables stabilise to the following values: (CO ↓ ↓ ↓, MAP ↓ ↓ ↓, HR ↑ ↑, EDP ↑ ↑).

Part of the simulation consists in generating a virtual patient's appearance that corresponds to its clinical status. This is done by mapping the physiological parameters to elements of visualisation, such as skin textures or patient's animations.

For instance, as cardiac output decreases so does cerebral perfusion: low CO values can thus be mapped to patient consciousness in the form of changing animations. Very high ventricular filling pressures result in elevated pulmonary capillary pressure, which can trigger cardiac edema, manifesting itself in the patient through altered breathing patterns.

However the most significant aspect of visualisation, as far as diagnosis is concerned, is that of physical signs. Skin tones depend on peripheral perfusion.

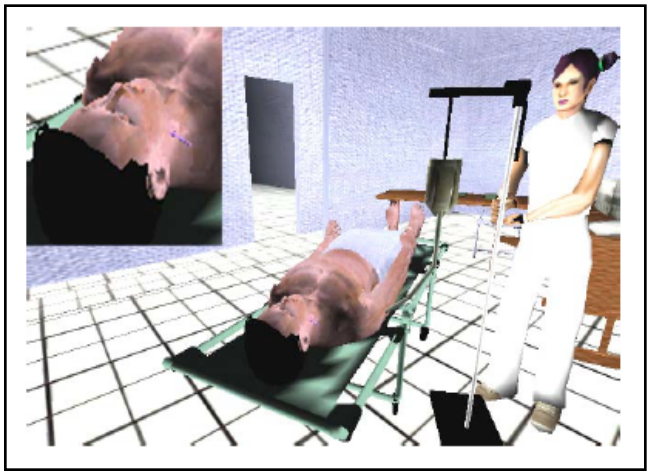

Figure 5. Distension of Jugular Veins as a Sign of Increased CVP.

Hence, vasodilation (decreased SVR) is accompanied by redness, while vasoconstriction results in intense pallor. The value of the SVR parameter is thus mapped to dynamic textures shifting between various skin appearances.

Finally, the effects of medical treatment are simulated by modifying the corresponding target variables on the pathophysiological model obtained from the first simulation and running the qualitative simulation again until a new steady-state is obtained, which corresponds to the effects of the therapy in that context (see Table I).

Table 1. Target Parameters of Some Common Treatments

Treatment	Target Parameter
IV Fluids	Blood Volume
_-agonist	Inotropism, HR
Vasodilator	SVR (_)
Norepinephrine	SVR (_)

The effects of the correct therapeutic, beta-agonist are shown on figure 4. They restore inotropism, ejection and a MAP closer to normal but still low. Heart rate remains high in the acute context and due to the side effect of the drug itself. End-diastolic pressure and PCap decrease. Conversely, fluid expansion initially increases ventricular venous return, but due to a low stroke volume, only contributes to a dangerous elevation of filling pressures and PCap, while cardiac output remains low. This triggers various clinical signs in the patient, such as changes in respiratory rate (onset of pulmonary edema) and under certain circumstances, distension of the jugular veins (Figure 5).

Conclusions

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. A realistic simulation should render the atmosphere and tension created by the critical nature of the situation. In that sense, the visual representation recreates some of the emotional tension of realistic situations.

References

1. Baan, J. Arntzenius, A.C., Yellin E.L. (Eds.) Cardiac Dynamics. Martinus Nijhoff, The Hague, 1980.

2. Badler, N.Webber, B.Clarke, J., Chi, D., Hollick, M., Foster, N., Kokkevis, E., Ogunyemi, O., Metaxas, D., Kaye, J. and Bindiganavale, R. MediSim: Simulated medical corpsmen and casualties for medical forces planning and training, National Forum on Military Telemedicine, IEEE, 1996, pp. 21-28.

3. Cavazza, M. and Simo, A. A Virtual Patient Based on Qualitative Simulation, ACM Intelligent User Interfaces 2003, Miami, FL, USA., pp. 19-25, 2003.
4. Escaffre, D. Qualitative Reasoning on Physiological Systems: The Example of the Blood Pressure Regulation. In: I. DeLotto and M. Stefanelli (Eds.), Artificial Intelligence in Medicine, Elsevier Science Publishers.
5. Forbus, K.D. Qualitative Process Theory. Artificial Intelligence, 24, 1-3, pp. 85-168, 1984.
6. Kuipers, B. Qualitative Simulation in Medical Physiology: A Progress Report. Technical Report, MIT/LCS/TM-280, 1985.
7. Lewis, M., Jacobson, J., Communications of the ACM, 45, 1, January 2002. Special issue on Games Engines in Scientific Research.
8. Long W.J., Naimi, S., Criscitiello, M.G., Pauker, S.G., Kurzrok, S. and Szolovits, P. Reasoning about therapy from a physiological model, in Proceedings of MEDINFO'86 (Washington DC).
9. Widman, L.E. Expert System Reasoning About Dynamic Systems by Semi-quantitative Simulation. Computer Methods and programs in Biomedicine, 29, pp. 95-113.