VIRTUAL PATIENTS BEHIND THE SCREEN USING COMPUTER SIMULATOR GOLEM

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Abstract: The authors have created an interactive multimedia computer simulator "GOLEM" for learning diagnostics and therapy of clinical disorders. It allows students to solve various critical situations in the form of simulation games. The simulator is based on mathematical simulation models of body-fluid balance, respiration, circulation and renal function. The mathematical description consists of 39 non-linear differential and algebraic equations of more than 200 variables. General aspects of large-scale model design and deployment are discussed. Typical usage of the simulator in medical training is described and its pedagogical benefits are highlighted.

Keywords: Computer Simulation, Educational Aids, Medical Applications, Physiological Models, Simulators.

1. SCHOLA LUDUS

The old credo "Schola Ludus" (or school through play in Latin), stated as early as the 17th century by Comenius, the founder of pedagogics, is coming true these days in interactive multimedia simulators. The connection of an interactive multimedia user interface with a simulation model offers students the possibility to explore the subject of examination in a virtual world. Participants of the "Simulation games" can test the behaviour of the simulated object without risk – one can train to land a virtual airplane as well as diagnose and treat a virtual patient with the possibility of changing decisions or starting again in case of failure.

Similarly to a flight simulator which is based on a more or less realistic model of a plane, there is a model of the human body (or some of its subsystems) behind a medical simulator. Advances in biological and medical modeling are closely related to a mathematically formalized description of physical reality – i.e. the transformation of a purely verbal description of the network of relationships to a description in the formalized language of mathematics.

Efforts in this field resulted in the international project PHYSIOME (www.physiome.org) which is a successor of the GENOME project. While the aim of the GENOME project was to map the human genome, the task of the PHYSIOME project is to describe the functionality of the human body in a quantitative, formalized manner.

With the possibility of commercial use of simulation models, there is a change in availability of the formalized physiological description, in the form of equations or algorithms, of a medical simulator. These equations and algorithms have turned from an object of scientific research to technological know-how, kept hidden from potential competitors.

While it was common to request the source code of a simulator at the end of the eighties, today it is not usually possible. E.g. for the medical simulators from Critical Concepts[1] Inc., Biological simulators Inc.[2] or Mad Scientist Software Inc.[3], there is only general information available on their theoretical basis.

The development of medical simulators in our laboratory is an open, non-commercial university project and the structure of the simulation models is available at our website[4].

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[1] www.laketech.com
[2] www.biosim.com
[3] www.madsci.com
[4] www.physiome.cz

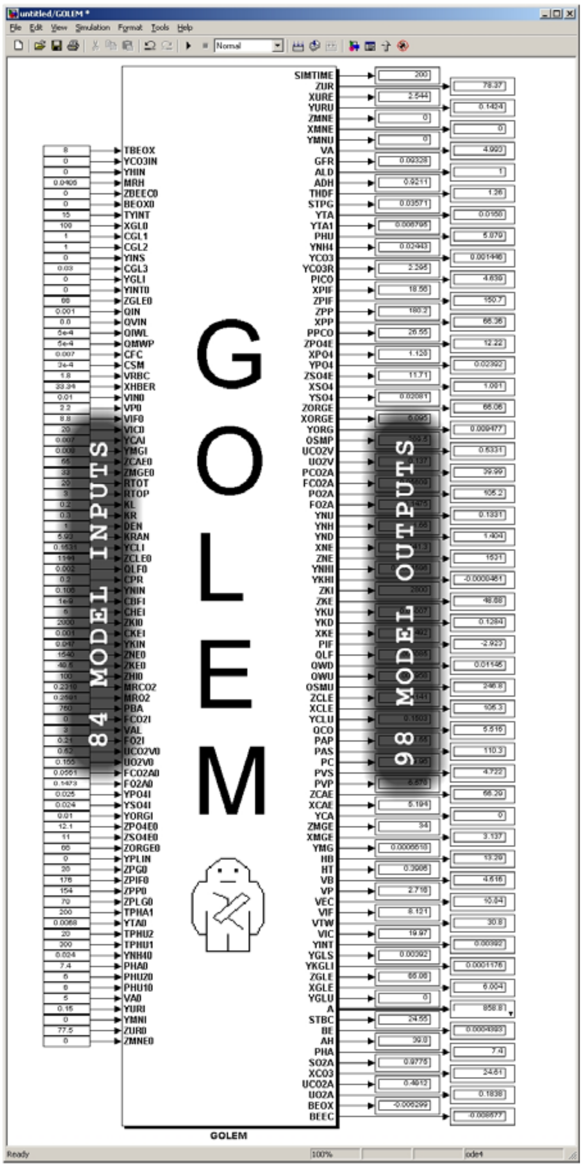

Fig. 1. Simulation chip containing the integrative model that serves as a framework for the simulator Golem. In the graphical environment of the Simulink, simulation model input values can be connected to separated "pins" of the simulation chips and the time-course of the corresponding variables can be registered on the virtual displays or oscilloscopes.

The basis of our educational simulator Golem is a simulation model that implements global physiological regulations – control of ionic, acid-base, electrolyte, osmotic and body-fluid volume balance; control of circulation, respiration and renal function including hormonal control (insulin, aldosterone, ADH and natrium uretic hormone). The model is quite large, consisting of 39 nonlinear differential and algebraic equations with 84 input and 98 output variables (see fig 1, 2). The detailed structure of the entire model, the complex scheme is available on the Internet at www.physiome.cz.

The simulation model of Golem has been developed in Matlab/Simulink® environment from Mathworks. The model is organized into subsystems, represented by so-called ***simulation chips*** in Simulink [Kofránek

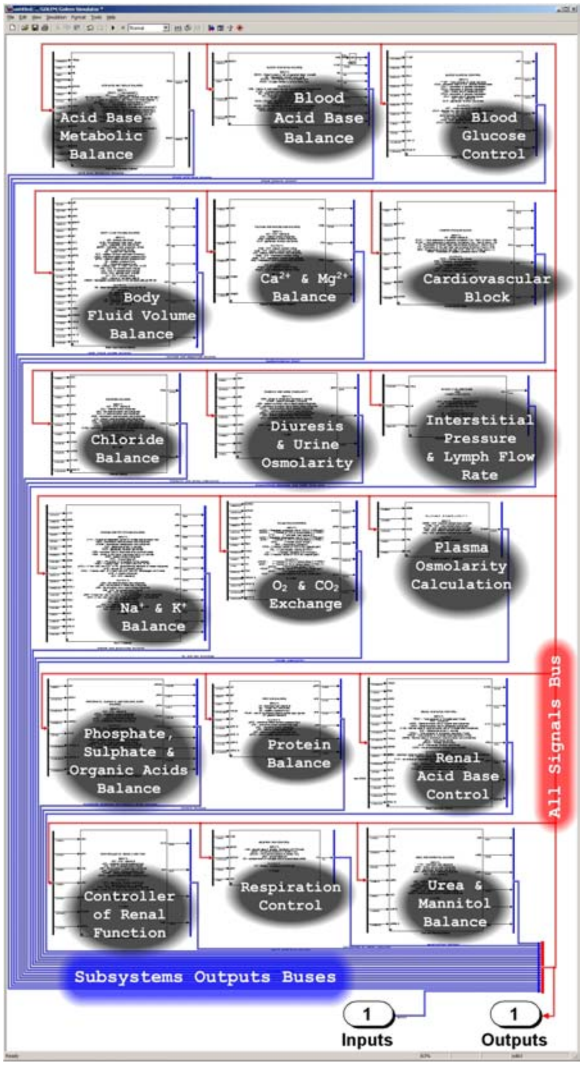

Fig. 2. The inner structure of simulation chip from fig. 1. The structure looks like an electronic circuit with interconnected chips, that are represented by simulation chips of a lower hierarchical level. Interconnected simulation chips depict the core structure of the large-scale model of physiological regulations

et. al 2002a]. by so-called ***simulation chips*** in Simulink [Kofránek et. al 2002a].

A simulation chip represents a subsystem with an exactly defined function. The mask (and help system) of this chip contains a brief description of its function and meaning, and a description of the inputs and outputs. Physiologists can look at this chip as like a black box with some physiological functions and programmers can look at the chip as like a subprogram or algorithm that is part of a more complex system. The simulator itself and its user interface have been created in Control Web from Moravian Instruments (see www.mii.cz), the tool for industrial measurement and control applications [Kofránek et. al 2000, 2001, 2002b].

2. LARGE-SCALE MODELS OF PHYSIOLOGICAL SYSTEMS

The behavior of the model behind an educational simulator must include concurrent effects of many

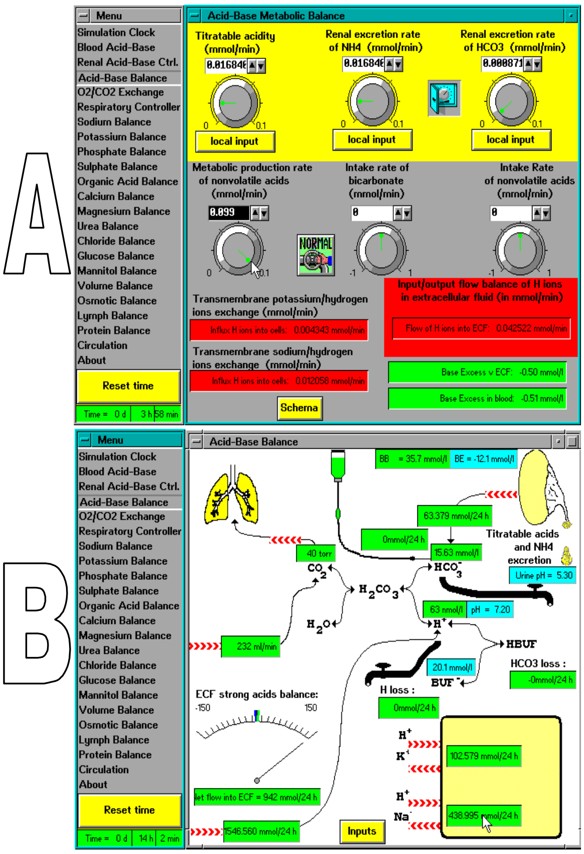

Fig. 3. Simulation of metabolic acidosis in the Golem simulator. (A) Turning the knob we can increase the metabolic production rate of non-volatile acids. By increasing the strong acid production, we cause metabolic acidosis. (B) The ratio of metabolic production and renal excretion of strong acids is highly increased. H^+/Na^+ and H^+/K^+ exchange on the cell membrane is activated. H^+ ions are buffered by intracellular and extracellular buffers.

physiological subsystems involved in the development of various pathological states – e.g. mutual interaction of circulation, respiration and renal function.

These large-scale models have many input/output variables and parameters. This brings complication when identifying the parameters of a model – it is not possible to obtain the time-courses of all physiological quantities from a patient, often they are only estimates. In large physiological models one often uses statistical values of respective quantities with corrections derived from global anthropometrical quantities – height, weight, sex etc. But every human is unique and so are his physiological parameters; although the structure of control loops is common for all.

Large-scale models usually have a hierarchic lumped parameter structure. The framework for the multimedia simulator "GOLEM" is the ***large varying-scale model*** consisting of minimalized interconnected models of the 18 subsystems (see fig. 2). The subsystem models allow switching between several models with different distinguishing levels of description. The level of details of a subsystem must

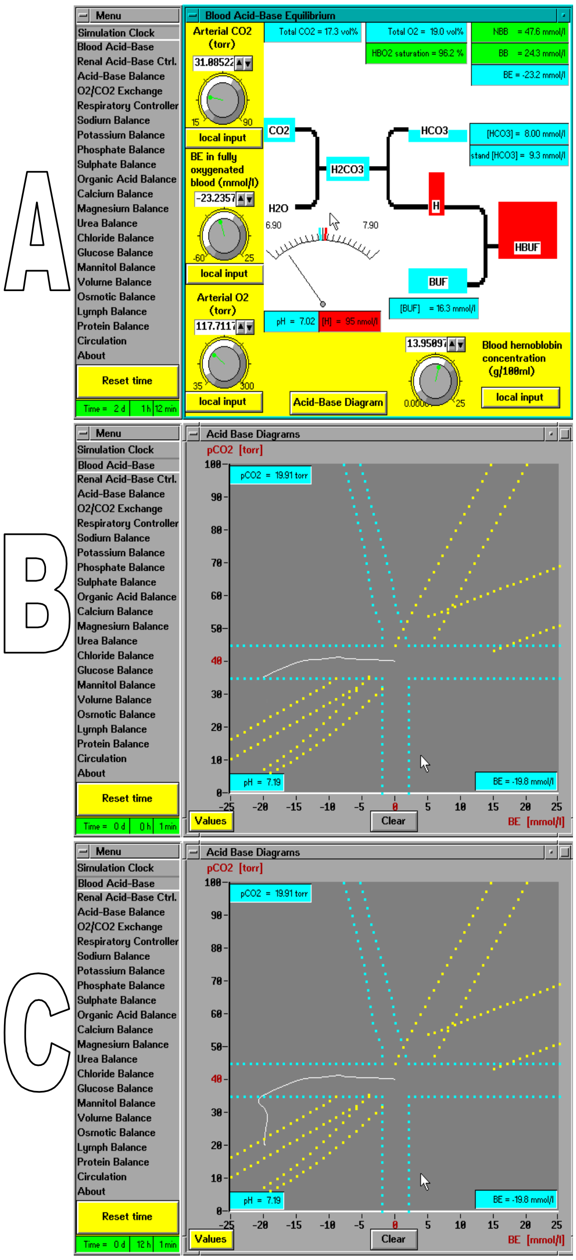

Fig. 4. Simulation of metabolic acidosis in the Golem simulator: compensatory responses of blood buffer system and respiration. (A) Blood buffer system - the blood has been acidified, Base Excess and actual bicarbonate concentration are decreasing, and pCO_2 is also slowly decreasing. (B) Acid-base values on this compensatory diagram are in the acute metabolic acidosis range. This is the beginning of a progressive reaction by the ventilation centre to counteract metabolic acidosis. (C) Respiratory compensation is at a maximum in about 12 hours. Decreasing pCO2 is leading to a rise of arterial blood pH. Acid-base parameters are approaching a compensated metabolic acidosis range.

be adequate to the educational purpose and must fit the other subsystems so that some part of the model is not too detailed while another is oversimplified. E.g. for the explanation of the role of ventilation–perfusion mismatch in respiratory disorders, lungs can be modeled as a series of many regions with the different ventilation-perfusion ratios, while in the large-scale models of kidney functions (where the detailed analysis of the mechanism of respiratory disorders is not the aim) the multi-compartment structure of the lungs can be approximated by more simple structure.

Different criteria are used when identifying large-scale and high level-of-detail models. In the large scale, it is not required that the outputs of the model precisely match the data measured on a particular patient. Semi-quantitative and qualitative criteria apply; the correspondence of trends to clinical experience is sufficient. See fig. 3-5 where the development of metabolic acidosis is explained.

Large-scale models of physiological systems were first published in the seventies and eighties [Guyton 1973, Amosov, 1977, Ikeda et al 1979, Coleman et al. 1983]. They played an important role in causal explanation of the development of pathololgical states. These models can explain the symptoms of respective diseases and how the individual control loops contribute to pathogenesis. For these reasons the large-scale models are suitable for educational simulators.

3. SIMULATORS INSTEAD OF PATIENTS

The graphical user interface of the Golem simulator is designed to be as interactive and user friendly as possible, see fig 3-7.

From the pedagogic point of view it is very effective to be able to **observe responses of individual physiological subsystems** to changes of quantities, which are controlled in other parts of the organism.

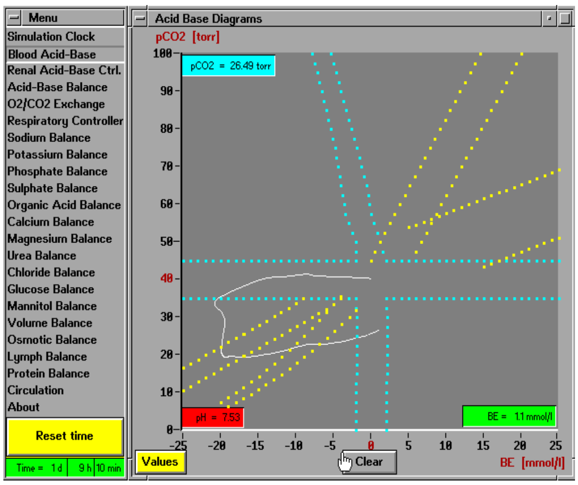

Fig. 5. Virtual therapy of metabolic acidosis in the Golem simulator: Base Excess and pH slowly increases after bicarbonate infusion. PCO_2 remains stable for a while, thanks to respiratory compensation, at its low level. We must take PCO_2 into account when choosing doses of alkaline infusion in order not to overdose. If we overdose the infusion, as shown above, we correct the Base Excess value, but hyperventilation leads the patient from acidemia to alkalemia, which can be dangerous.

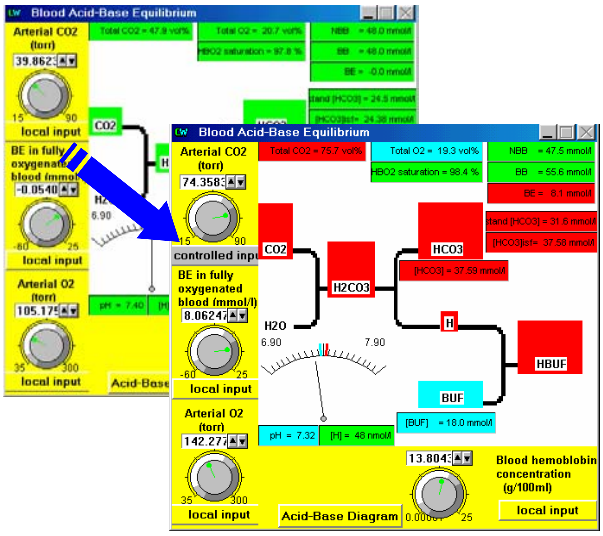

Fig. 6. PCO2 is disconnected from the regulation (e.g. from the influence of ventilation) – we can change PCO2 level (pCO2 is switched to local input) and look how the rise of PCO2 increases bicarbonate and decreases non-bicarbonate buffer bases (BUF$^-$). Behaviour of blood buffer system (independently of other subsystems of acid-base regulation) can be explored.

Therefore, we have introduced the **possibility of detachment** of some controlled variables **from the control loop** so that their input values can be set locally. A single push of a button corresponding to the appropriate variable, which is an input to a subsystem, immediately disconnects the variable from the outer regulatory loop. This allows the experimenter to focus on a specific physiological subsystem during the simulation and **study its behaviour independently of the complicated regulation relationships** inside the whole organism and separately from other subsystems. This enables **better understanding** during the study. After pushing the corresponding button the variable is connected to the regulatory loop again (see fig. 6).

By disconnecting the individual regulators we can observe separately the behaviour of independent regulatory loops and partial physiological subsystems. Thus, the **simulator substitutes for the whole scale of models of partial physiological subsystems** and it can contribute to the understanding of a single physiological regulatory link. With the help of simulation games with progressively interconnected subsystems, the student acquires a dynamic perspective of the relatively complex problems of the homeostasis of the internal environment, which is very important in better understanding of the dynamical mutual relations between the regulations of acid-base, ion, osmotic and volume homeostasis. For example, the student can step by step observe, how high aldosterone level can causes metabolic alkalosis (see fig. 7).

4. CONCLUSION

The Golem simulator is a multimedia tool intended to support training in pathological and clinical

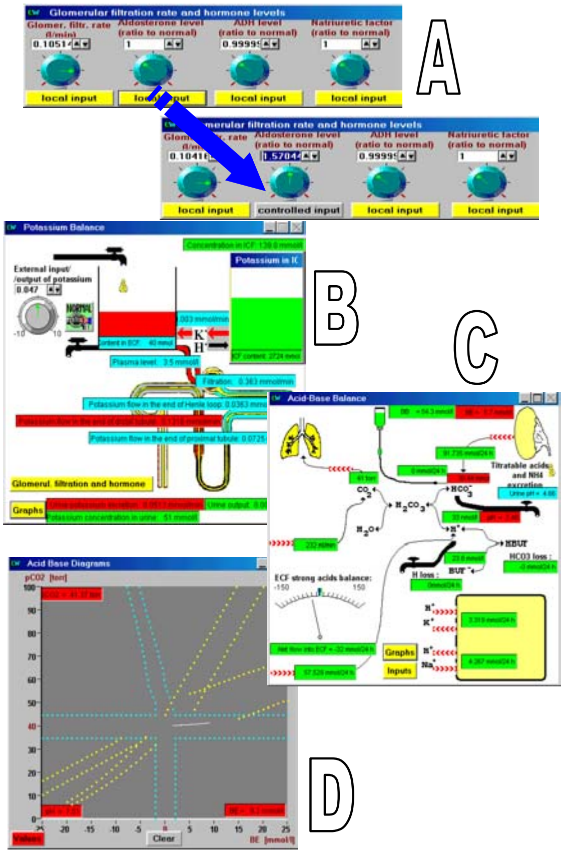

Fig. 6. Aldosterone has been disconnected from regulation of its level. We can manually increase the aldosterone level (A). Renal potassium excretion increases in response to high aldosterone level. (B). Potassium leaves the cells and exchanges with hydrogen ions. There is the negative balance of hydrogen ions in the extracellular fluid (C). Metabolic alkalosis slowly develops as a result of high level of aldosterone, as we can see on the Acid-Base compensatory diagram (D).

physiology. Golem allows the setting up of various scenarios – e.g. diarrhea, vomitus, renal disorders etc. Students then can examine the role of individual control loops in the pathogenesis of complex disturbances of body-fluid homeostasis, respiratory and circulatory insufficiency and the response of the organism to therapy.

The disorders of acid-base, ionic and osmotic balance are often treated separately in classical textbooks. In clinical practice these disorders usually come hand in hand. Thanks to the complexity of the simulator, students can examine the homeostasis disturbances in any context. There is the possibility of watching the combined response of many control loops to a pathological condition. On the other hand, Golem allows the disconnection of individual physiological subsystems and studying their behaviour separately, in accordance with the *from simple to complex* pedagogical principle.

The trade-off for the complexity and extent of the simulator is the demand on the preparation of the training. Golem does better as a teaching aid in a teacher-guided seminar than as a standalone e-learning tool for distant self-study.

The future work of our team is directed towards devising *multimedia educational applications* based on the Golem simulator, focusing on the explanation of the pathological and clinical physiology of body-fluid homeostasis and cardiorespiratory disorders.

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ACKNOWLEDGEMENT

This research was partially supported by the Research and Development Initiative MSM 111100008 (physiome.cz) and by BAJT servis Ltd.