GOLEM - Multimedia Simulator for Medical Education

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Abstract

We created multimedia medical training simulator "GOLEM" for learning diagnostics and therapy of the critical clinical disorders. The theoretical basis of the simulator is the mathematical formulation of the relationship of homeostasis of the internal environment (acid/base and electrolyte equilibrium, of transport of blood gases, of osmotic and volume homeostasis), respiration, circulation and kidneys including regulatory influence of relevant hormones and the influence of some therapeutic procedures. Mathematical description consists of 39 non-linear differential equations and containing 89 input and 179 output variables. For the development of the simulation models developer's tools from MathWorks (Matlab and Simulink) has been used. The integration of the multimedia components, hypertext and simulation models interface was achieved by using Control Web, developed by Moravian Instruments, originally designed for long distance controls using PC and Internet. We have used our simulator as an efficient educational tool to help medical students learn circulatory, respiratory, acid-base, electrolyte, osmotic and volume disorders and train the diagnostic and therapeutic decisions by executing simulated interventions on virtual "patients".

Keywords:

Models Educational, Computer Simulation, Hypermedia, Acid-Base Equilibrium, Water-Electrolyte Balance.

Aim of the project

The author's intention was to create the *multimedia medical simulator as an interactive teaching tool* to help medical students learn acid-base, electrolyte, osmotic and volume disorders, respiratory and circulatory insufficiency. Our ambition was to allow students training in diagnostic and therapeutic decision-making process by executing simulated interventions on virtual "patients".

Materials and Methods

Two different, but consequential tasks must be solved when developing a medical simulator

1. The development of the simulation model of

- *physiological functions* the theoretical work itself, based on formalization of physiological relations.
- The development of the simulator of physiological functions (the working title "GOLEM" is used) and the use of the simulator in education – practical application of the theoretical results. In addition, we have always supported the Internet accessibility of the project results.

Each of the problems is specific and requires using different developer's tools.

Simulation model design with simulation chips

Whereas developing an educational simulator is a programmer's work, formalization of the physiological relations is rather than creating software complicated scientific problem. To solve that effectively adequate tools are needed. Luckily for us, in the last few years substantial progress has been made in the field of software development tools for the design and testing of simulation models and we could utilize the advantage of professional tools by Mathworks (Matlab, Simulink and related libraries). These tools allow creating simulation models in an easy way illustrating their structure graphically as linked simulation circuits associated into "simulation chips". In the same way as in electrical circuits electrical current is conveyed, in simulation chips information about the values of the variables is carried. The behavior of the "software chips" can be easily tested with the help of adequate software tools for computer simulation: similarly to an electric scheme, where it is possible to carry current on individual "pins" of the chip, the same manner can be used to carry selected value (or some time course of values) of an appropriate variable to the software chip. At the same time "measuring displays" can be "connected" to the outputs to register the values as long as the simulation is running.

Importantly, schematic representations using simulation chips are understandable for physiologists. It seems therefore that expression of the simulation models of physiological systems with the interlinked simulation chips could be a suitable way of standardization.

Simulator design with industrial developed tool

When generating a simulator we face a rather difficult task.

On one hand, we need to create a comprehensive graphical interface (with the integration of interactive animations, charts etc.). On the other hand, the structural complexity of the simulation model (which is the heart of the simulator) has high demands on the numerical performance. The requirements for sophisticated graphics and the demands on the high numerical performance of the running complex simulation model are contradictory – both are demanding on the processor performance.

When searching for the acceptable developer's software tools for the development of the simulator we have looked in a field, where analogous contradictory requirements can be met. We have found one such a field and that is the generation of controlling and measuring applications for the industry. Here, similarly, the primary goal is to maintain high numerical output for the control and measuring application (which cannot be interrupted by drawing the graphics) even with the requirements for the graphical level of the user interface. After a certain time of searching, we have chosen the *Control Web* developer's environment by *Moravian Instruments*.

When incorporating the simulation model into the core of the generated simulator the following trick was used: instead of the measuring/controlling adapter driver by which Control Web communicates with an industrial device in an industrial application, we have programmed a virtual driver for an (nonexistent) measuring/controlling adapter that was based on the simulation model. The Control Web application now "thinks" that it sends some controlling signals through the driver to an industrial device, but in reality the signals are inputs into the simulation model. Similarly, instead of measured output signals from the periphery, the Control Web application registers the values of the output variables of the model. This allowed us to employ the abundant options of the Control Web developer's environment for the generation of our own simulator. The generation of the simulator is also facilitated by the options of the Mathworks special toolbox that allows automatic conversion of the graphical schemes from Simulink (the simulation circuits) into the source code of the program in C++.

Results

The *theoretical concept* of the simulator GOLEM is the large simulation model based on mathematical formalization of the blood gasses transfer, acid-base, electrolyte, volume and osmotic equilibrium, the function of the respiratory and urinary system, including the influence of hormones. The model design is based on classical models of Guyton et al. [3,4], Cameron [1], Ikeda ett al. [5] and Coleman et al. [2], which we have sufficiently redesigned and extended. It consists of *39 non-linear differential equations* and contains *89 input and* 179 output variables.

The simulator GOLEM enables to visually demonstrate the mutual relations between the individual physiological subsystems and the manifestation of these relations in individual pathological conditions. The simulator enables

the computer modeling of various pathological conditions and the influence of appropriate treatment. The simulator therefore becomes a visual learning aid for better understanding of the nature of physiological regulations and the manifestation of their malfunctions.

In connection to the development of distance studies via the Internet, we would also like to create an Internet version of the simulator, which would be accessible from an outside computer via a standard web browser. Simulator is drawn up so that its controlling would be as easy as possible.

The following simple example of an acid-base disorder should demonstrate how easy it is to manipulate the simulator. By changing the value for metabolic production of strong acids we can cause a metabolic acidosis in our "virtual patient" (fig. 1).

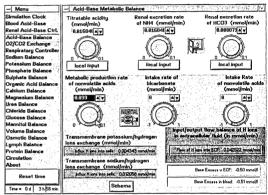


Figure 1 – Turning the knob we can increase the metabolic production rate of non-volatile acids.

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. Intracellular and extracellular buffers buffer H^+ ions (fig. 2).

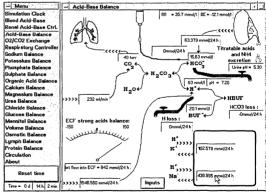


Figure 2 - Acid-base balance in acute metabolic acidosis.

Our "virtual patient" is showing signs of metabolic acidosis - the blood has been acidified, Base Excess and actual bicarbonate concentration are decreasing, and pCO₂ is also slowly decreasing (fig. 3).

Acid-base values on compensatory diagram are in the acute metabolic acidosis range. This is the beginning of a progressive reaction by the ventilation center to counteract metabolic acidosis (fig 4). 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 (fig.

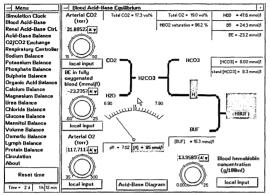


Figure 3 – Blood acid base equilibrium in acute metabolic acidosis.

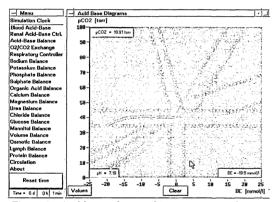


Figure 4 – Acid-base values on this compensatory diagram are in the acute metabolic acidosis range.

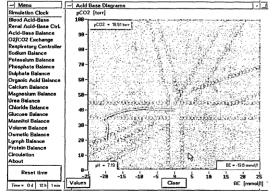


Figure 5 – Acid-base parameters are approaching a compensated metabolic acidosis range

5). The slow response of the respiratory system on metabolic acidosis is due to the relative impermeability of bicarbonate across the blood-brain barrier (fig. 6). While CO_2 penetrates easily and pCO_2 in blood and cerebrospinal fluid is at a similar level, this is not the case for bicarbonate. Thus bicarbonate reaches equilibrium, cerebrospinal pH decreases, and the respiratory center is

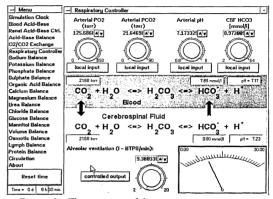


Figure 6 – The response of the respiratory system on metabolic acidosis is developed.

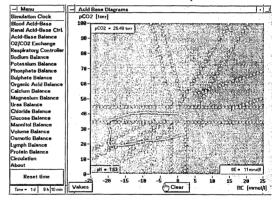


Figure 7 – The kidney's response progressively develops. Turning the knob we are starting bicarbonate infusion.

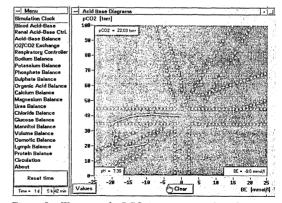


Figure 8 – We must take PCO₂ into account when choosing doses of alkaline infusion in order not to overdose.

more stimulated, and alveolar ventilation increases resulting in a decrease of pCO₂. Values of acid-base parameters are slowly approaching to compensated metabolic acidosis range. The kidney's response progressively develops. Titratable acidity and NH₄ excretion increases, urine pH decreases. Renal response is in its maximum in 3-5 days (fig. 7).

The simulator allows "virtual therapy" so that we can start an alkaline infusion for metabolic acidosis. To help the strong acid input/output balance, we can start bicarbonate infusions by simply adjusting the appropriate rate of bicarbonate intake in the simulator and alkaline infusion therapy of metabolic acidosis of our "virtual patient" is initiated (turning the knob we are starting bicarbonate infusion therapy - see figure 7).

BE and pH slowly increases after bicarbonate infusion. PCO₂ remains stable for a while (thanks to respiratory compensation), at its low level. We must take PCO₂ into account when choosing doses of alkaline infusion in order not to overdose (fig. 8).

In virtual therapy we can allow ourselves to make a mistake such as overdosing the alkaline infusion which in real life can be dangerous. If we overdose the infusion (fig. 9), we correct BE, but hyperventilation leads the patient from acidemia to alkalemia, which can be dangerous.

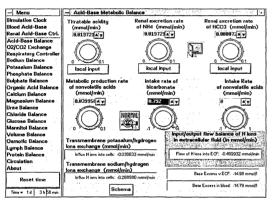


Figure 9 – Alkaline infusion has been overdosed.

During acidemia (see figure 2) the cell membrane exchanges potassium ions for hydrogen ions entering into cells to be used by buffers. If acidosis lasts too long, the supply of potassium in the cells decreases, resulting in the depletion of K^+ . Inadequate therapy would quickly lead the patient from acidemia to alkalemia, as the cell exchanges K^+ for H^+ (from the intracellular buffers). Because extracellular stores of potassium are limited, its plasma concentration will quickly and dangerously decrease. (see figure 10).

It is necessary to replace lost potassium. We can then try correcting it, or simply pressing "Restart" button to try the all simulation run again. To correct the K^+ depletion, we must use a potassium infusion in glucose and insulin insulin takes glucose into cells but also increases the entry of potassium into cells resulting in a faster correction of K^+

depletion (fig. 11). The infusion must not contain too large concentrations of potassium (as this would increase K^+ to dangerous level).

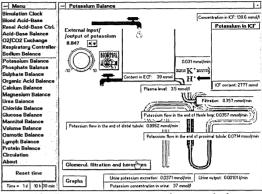


Figure 10 - Potassium concentration dangerously decreases.

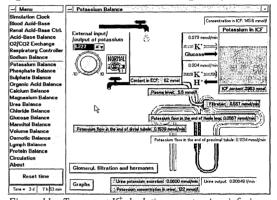


Figure 11 – To correct K⁺ depletion, a potassium infusion in glucose and insulin is used: - insulin takes glucose into cells but also increases the entry of potassium into cells resulting in a faster correction of K⁺ depletion.

A mistake is no reason to get upset since the patient is virtual (and so his death is just virtual). A real patient would not take our carelessness so easily, however. The simulation can be stopped at any time by using the Stop "switch" on the simulation clock and we can then take our time to analyse the many variables in the individuals physiologic subsystems windows.

Discussion

The simulators bring entirely new possibilities into the education of physicians. Not only they allow the students to try various therapeutic interventions (and to return to the starting point if necessary) without any threat for the patient, but also they are helpful teaching tools for gradual explanation of complex physiologic regulatory relations.

We can disconnect individual physiological subsystems (only on computer, not in reality, obviously) from their regulatory loops and observe their actions separately. In the "simulation game" with the individual subsystems, the

student can better understand the importance of the individual physiological relations and their involvement in all sorts of pathological conditions. That is why we have enabled the disconnection of the regulatory loops of each subsystem in our simulator of physiological functions GOLEM so that their behavior can be observed separately.

With the help of the 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 greatly important in the 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 (fig. 12).

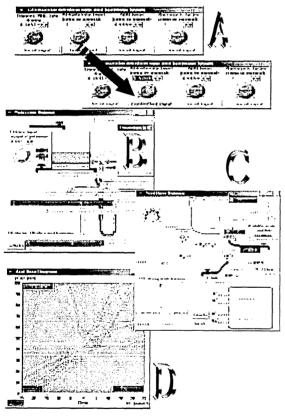


Figure 12 - Aldosterone has been disconnected from regulation of its level. We can manually increase the aldosterone level (A). Renal potassium excretion increases in response to high aldosterone level. (B). Potassium leaves the cells and exchanges with hydrogen ions. There is the negative balance of hydrogen ions in the extracellular fluid (C). Metabolic alkalosis slowly develops as a result of high level of aldosterone (as we can see on Acid-Base compensatory diagram) (D).

Conclusion

We have tested our simulator and multimedia computer aided learning tool in educational practice of our faculty. It seems that *multimedia combined with the simulation* are becoming an *efficient teaching tool* to help medical students in learning complicated pathophysiological disorders. Due to the interactive features of the simulation model user interface, it enables a *better perception* of the complicated dynamic relationships within complex physiological structures.

Acknowledgments

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References

- [1] Cameron WH. A Model Framework for Computer Simulation of Overall Renal Function. *J. Theor. Biol.* 1977: 66, pp. 552-572.
- [2] Coleman TG and Randall JE. HUMAN. A Comprehensive Physiological Model. *The Physiologist* 1983: 26, pp. 15-21.
- [3] Guyton AC, Coleman TA, and Grander HJ. Circulation: Overall Regulation. Ann. Rev. Physiol. 1972: 41, pp. 13-41.
- [4] Guyton AC, Jones CE and Coleman TA. Circulatory Physiology: Cardiac Output and Its Regulation. Philadelphia: WB Saunders Company, 1973.
- [5] Ikeda N, Marumo F and Shirsataka M. A Model of Overall Regulation of Body Fluids. Ann. Biomed. Eng. 1979:7, pp.135-166
- [6] Kofránek J, Velan T and Kerekeš J. Golem: A Computer Simulator of Physiological Functions as an Efficient Teaching Tool. In: Teo ZM., Wong. WC, Oren TI and Rimane R, eds. Legacy for 21st Century. Proceedings of the First Word Congress on Systems Simulation., Singapore: IEEE Singapore Section, 1977; pp. 407-411.
- [7] Kofránek J, Velan T and Janicadis P. Computer Simulator of Body Fluids and Acid-Base Disorders as an Efficient Teleeducation Tool. In: Carson E and Salzeider E, eds. Modelling and Control Biomedical Systems 2000. IFAC Symposium. London: Pergamon, 2000; pp. 233-242.
- [8] Kofránek J, Velan T, Janicadis P and Kerekeš R.: Golem – medical multimedia training simulator of body fluids and acid-base disorders. In: Waite W and Nisanci A, eds. *The Proceedings of 2000 Summer Computer Simulation Conference*. Vancouver: SCSI, 2000; pp. 736-741.

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