FUNCTIONAL ANATOMY OF FULL-SCALE PATIENT SIMULATORS

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INTRODUCTION

Originally created as full-scale anesthesia simulators [1–4], these state-of-the-art learning systems have evolved significantly over the past decade to become patient simulators. Full-scale patient simulators help not only anesthesiologists, but a wide variety of medical practitioners and students learn the diagnosis and management of clinical problems without risk to real patients [5, 6].

The success of a simulation exercise depends on design decisions at many levels. In a description of computer simulated patient-physician encounters [7], Friedman states, "Simulator designers must decide which features of the complete patient should be included, which features should be purposefully excluded, and how those included should be presented to the users." In the context of full-scale patient simulation, four specific design levels can be identified. The *hardware* design includes the patient mannequin, exterior features, clinical signs representation, mechanical models, and computer systems. The *software* design includes the user interface, mathematical models, model parameters, communication protocol between computers, code structure, and programming language. The *curriculum* design includes the target learners, educational needs assessment, learning objectives, patient types, clinical scenarios, and formal evaluation methodology. The *exercise* design includes the number of participants, pace, modulation of severity, student-instructor interaction, and performance evaluation. Simulator hardware and software design decisions are usually made by simulator developers, while curriculum and exercise design decisions are made by clinical instructors. In this paper, we describe the major design considerations made by the simulator developer (hardware and software). Others have previously described curriculum and exercise design decisions made by clinical instructors [8–10].

We focus on design decisions concerning the full-scale simulator "engine," the component of the simulator that generates the physiologic and pharmacologic responses of the simulated patient. In the first two sections, general design considerations are discussed, such as the use of scripts or models to control the simulator,

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and the interfacing of mechanical and mathematical models. In the last section, we use the full-scale simulator developed at the University of Florida (Medical Education Technologies, Inc., Human Patient Simulator [UF-METI HPS], Sarasota, Florida) as a specific, real-world example to illustrate concepts that are applicable to all full-scale patient simulators.

Understanding the entire multi-level design decision process is a prerequisite to informed discussions between clinical instructors and simulator developers about the strengths and limitations of current full-scale simulators. Empowered with the concepts presented in this paper, interactions between clinical instructors and simulator developers will shape future design decisions, and result in enhancements, new configurations, and new educational applications of full-scale patient simulators.

SCRIPT-CONTROLLED VS. MODEL-DRIVEN SIMULATION

Most clinical learning objectives in anesthesiology and critical care have in common the need for realistic cardiovascular and respiratory responses to intravenous fluid management, artificial mechanical ventilation of the lungs, and drug administration, both in normal and pathophysiological situations. Two distinct approaches to generating these simulated patient responses automatically (without the intervention of a simulation director) are described.

The first is a simulation script, a set of commands that cause the patient simulator to operate in a specified manner. The script must anticipate actions and interventions by the trainee and simulate the patient's physiological response [3]. The script-driven approach has the advantage of being explicit and unequivocal with respect to generated responses. Scripts can describe responses to events that can be characterized by their occurrence and time sequence, for example, laryngoscopy, endotracheal intubation, and aortic clamping. The influence of one single management variable, for example, the cardiopulmonary side effects of an intravenous hypnotic, can still be taken into account by using a script. In this case, the script has to "spell out" responses to fine increments of the administered dose. Elaborating on this example, the script should specify that laryngoscopy following a small ("inadequate") dose of hypnotic results in tachycardia and increased blood pressure while an excessive dose ("overdose") of hypnotic results in decreased blood pressure. In a similar way, the evolution and influence of a single "internal" variable can be simulated using a script, for example, the onset and expansion of a pneumothorax and its influence on chest movement and gas exchange. Some of the dynamic (time) aspects of patient responses to therapy can also be taken into account by a script. In general however, a scripted simulation cannot be designed to anticipate all possible management options, all possible, and potentially valid, dosing schemes (repeated boluses and infusions) devised by different trainees, nor sort out the cardiovascular and respiratory responses to each of them.

Model-driven simulation, as opposed to script controlled simulation, has the potential to represent management variables as continuous values that change with time. More importantly, model-driven simulation can more readily be designed to react to the multitude of management options, and to represent the possible interactions between different physiologic subsystems. Consider the multiple management options for hypotension: intravenous fluid management, patient position, cardiac inotropes, and peripheral vasoconstrictors. The different responses not only depend on the timing, magnitude, and combination of the management variables, but also on the underlying cause of the hypotension. Scripting of all possible responses is virtually impossible. Another illustrative example is the rebreathing of CO_2, which causes an increased alveolar partial pressure of CO_2 (PCO_2) that influences the systemic uptake and distribution of that gas in the body tissues. This leads to a higher PCO_2 in the brain, and if the CO_2 response is not blunted by a respiratory depressant (depending on pharmacokinetics, pharmacodynamics, and control of breathing), the higher PCO_2 will result in an increased ventilatory drive. This, in turn, causes an increased respiratory muscle pressure, which results in larger fluctuations of the intrathoracic pressure and, thereby, influences the central and systemic blood pressures, which can then activate the baroreflex, and generate a respiratory sinus arrhythmia. It is difficult to imagine how this chain of potential reactions and interactions between physiologic subsystems, which results from numerous continuous management variables, can be implemented by a script, or for that matter, foreseen by a simulation director in real time.

It should be clear from the above examples why the control of patient simulators by a script alone has gradually been enhanced by a combination of mechanical and mathematical models. Integrated models of human physiology and pharmacology are an alternative, albeit more complex, solution to the problem of creating realistic responses to a multitude of dynamically interacting continuous variables. This was recognized even by the first developers of anesthesia simulators [1]. Others have described the use of integrated mathematical models to predict patient responses in a computer-

based (screen-only) simulation tool [11, 12]. Combining the convenient aspects of script control with the power of model-driven simulation, most full-scale patient simulators now have an engine consisting of integrated physiological models with independent variables and parameters that can be controlled by an instructor, either in real time through a console or via an educational exercise specific script file. We refer to this design as a "script-controlled, model-driven" simulator.

INTERFACING MECHANICAL AND MATHEMATICAL MODELS TO THE ENVIRONMENT

From the preceding description, the importance of physiologic and pharmacologic models for automatically determining the simulated patient responses to user actions and therapeutic interventions becomes readily apparent. To create a functional simulator system, these models must be interfaced to the user and to real world equipment, which can be accomplished with either realistic physico-chemical interfaces, or with artificial interfaces.

The use of real physico-chemical entities, such as electrical current for the electrocardiogram and real gases for the simulated lung, adds significant realism to full-scale simulation, enabling the simulator to interface with standard, real world medical equipment, such as monitoring instruments, mechanical ventilators, and other life support systems. An alternative method is to sense therapeutic interventions, and to stimulate monitors artificially, electrically, or electro-mechanically. Consider the example of arterial blood pressure. The most realistic interface is created when the arterial blood pressure (calculated by a mathematical cardiovascular model) is used to create hydraulic fluid pressures in a fluid-filled mannequin or mannequin component, such as the arm. Trainees cannulate the simulated radial artery and connect the catheters to a standard pressure transducer and physiologic monitor, no different than is done with a real patient. Artificial monitor interfaces include 1) electro-mechanical: direct connection of the (external or internal) electrical cables of the physiologic monitor to a circuit controlled by the computer running the mathematical cardiovascular model, 2) emulated: graphical display of the arterial blood pressure waveform on a separate artificial monitoring instrument emulator, or on the screen of the computer running the cardiovascular model, and 3) alpha-numerical: display on a computer screen of waveform parameters (systolic-diastolic-mean) in the form of (alpha-)numerical data. A similar classification can be made for sensing therapeutic interventions.

For most educational applications, the preferred form of creating clinical signs, such as heart and breath sounds, chest movement, and skin temperature, is through use of real physical entities such as actual sound, movement, and heat, respectively. This allows the trainees to use their own senses. Emulation using a multi-media computer, and alpha-numerical display are two artificial interface modalities that can be used for clinical signs.

Some of the physico-chemical interfaces serve as mere input or output devices to mathematical models. For example, in most simulators, a mathematical ECG model sends data to a digital-to-analog converter, which transmits the data to chest electrodes. Other models are implemented as hybrid (mathematical-mechanical) models. In most full-scale simulators, pulmonary gas exchange and lung mechanics are simulated using bellows or bags to represent the alveolar space, which are connected to the mannequin head by an anatomically realistic upper airway. In general, hybrid models are designed to simulate essential physiologic system dynamics and to directly provide a physico-chemical interface to the environment. Problems related to the implementation of physiologic models in hardware, include engineering challenges of construction, and the limited flexibility to change the parameters determined by fixed mechanical components. For example, it is difficult to realistically simulate the lungs of an infant using a 2-liter bellows.

Mathematical models, which rely on software to predict the simulated patient's responses, have more flexibility for changing parameters. For example, when simulating the cardiovascular system using software, a complex cardiovascular situation, such as hypotension, can be simulated simply by changing two of the model parameters, systemic vascular resistance and venous capacitance. Although feasible, this is much more difficult to accomplish in a mechanical (hydraulic) cardiovascular model with fixed component sizes. Most full-scale simulators have tools to help the clinical instructor change physiologic model parameters, such as O_2 consumption and baseline systemic vascular resistance, so that a particular patient or scenario can be created and tailored to the needs of a particular educational exercise [13].

Sometimes it is possible to derive a mathematical model by deduction only, based on the underlying physical laws and known parameters. Such a model is called a white box model. For example, models of electronic circuits are often white box models. In other situations, almost no prior information is available, and the model has to be derived from the measured data of input and output signals, without any information concerning the internal structure and internal relations.

These models are called black box models. Economic models are often black box models [14]. Most models used in medical education simulators are "gray box" models; some, but not all, model structures and parameters are derived from physical (anatomic, physiologic, pharmacologic) knowledge. Other parameters need to be adjusted or derived experimentally. As a general rule, the white box models respond more realistically to a wider range of input variables, and are better suited to represent interactions with other models. The disadvantages of white box models are related to their size: it may not be possible to obtain all model parameters for all possible situations to be simulated, and the computational efficiency is usually lower than that of a smaller black-box model. The choice between two models that simulate the distribution and elimination of intravenous drugs, representing different shades of gray, is discussed in the last section of this paper.

Most full-scale simulators use a mix of mechanical and mathematical models, and physico-chemical and artificial interfaces. This mix results from design decisions taken at the hardware and software levels, as mentioned in the introduction. These decisions greatly influence the capabilities of a particular simulator and the character of a simulation exercise.

INTEGRATED MODELS IN A FULL-SCALE PATIENT SIMULATOR

The models of the UF-METI HPS are based on the multiple modeling approach pioneered by Beneken and Rideout [15] and used in the software-only educational simulations [11, 12]. We enhanced the traditional multiple modeling approach by using a real physical system to model the pulmonary gas exchange and the lung mechanics of the simulated patient. The principal advantages of the resulting hybrid (mathematical-mechanical) lung model are that the simulated lungs can be ventilated using real gases and mechanical ventilators, and that standard, unmodified monitoring instruments can be connected to the simulated patient in the same manner that they are connected to real patients. The hybrid model also partially avoids the potential disadvantage of a pure mechanical system, specifically, less control over model parameters, by incorporating as many parameters as possible in the computer control part, rather than in the hardware implementation. Examples of such parameters include shunt fraction, and lung-thorax compliance. Except for the hybrid lung model, all other simulator models are mathematical models. Some models have physico-chemical interfaces, others have artificial interfaces. To understand how the METI-UF HPS works and how it can be used optimally, one must understand the inputs, outputs, and interactions between the models.

Table 1 lists the five models in the current HPS that receive real time data generated by the trainee in the management of the simulated patient and ventilator. The type of model and the different forms of interfaces, varying from physico-chemical interfaces to alpha-numerical data entry, are indicated. For several input modalities, alpha-numerical data entry is provided in addition to automatic sensing, creating an instructor override feature. For example, inflation of the wedge balloon on the pulmonary artery catheter is automatically sensed by the simulator, using an electro-mechanical linkage. When inflation is sensed, the pulsatile pulmonary artery pressure waveform is transformed into an appropriate "wedge" waveform. A data override from the instructor's console is also available. Using this, the instructor can "wedge" the pulmonary artery catheter even though the trainee has not inflated the wedge balloon, creating the clinical situation of a pulmonary artery catheter that has been inserted too far. Physico-chemical input, and electromechanical sensing of therapeutic interventions are always the preferred modes of data entry for realistic full-scale simulation, but are often more costly. In an attempt to balance the perceived educational benefits and the engineering resources necessary for development, we used physico-chemical sensing of therapeutic interventions for a subset of the models for the UF-METI HPS, and left other inputs at the alpha-numeric interaction level (Table 1).

Table 2 lists the outputs from the models to the monitoring instruments and clinical signs on the patient mannequin. Like the model inputs, the outputs vary from physico-chemical entities to numerical data. Unlike the ECG, which is transmitted to the chest electrodes as real electrical current, the numerical blood pressure data is converted to an analog electrical signal that directly stimulates the physiologic monitor. Likewise, the pulse oximeter does not measure the time varying absorption of two wave lengths of light, but is stimulated using an artificial electrical interface. The mathematical cardiovascular model contains an electrocardiogram generator that is in synchrony with the blood pressure wave forms, heart sounds, and palpable pulses. Physico-chemical entities and electro-mechanical stimulation are the preferred modes of data output for full-scale patient simulation. The selection of data output method ultimately reflects a balance between perceived educational benefits and engineering resources necessary for development.

The ensemble of mathematical and hybrid models and their interactions is referred to as the simulation engine (Table 3). Because of the multitude of possible

Table 1. Inputs from the simulation environment to the mathematical and hybrid (mathematical–mechanical) models of the UF-METI HPS

Model	Inputs	Interface type and implementation
Cardiovascular (MM)	Blood volume	EMI: fluid administration simulated by the scanning of a bar-code on a 250 ml bag of Ringer Lactate, and ANI
	Position of arterial, pulmonary artery, and central venous catheters	ANI
	Wedge balloon inflation	EMI: automatic detection of the inflation of the balloon of a pulmonary artery catheter already in place on the mannequin, and ANI
Lung mechanism (HM)	Airway pressures and flows	PCI: the inputs result in real gas pressures and flows in a pneumatic system, containing an anatomically correct upper airway, computer controlled airway resistance, and bellows representing alveolar volume with computer controlled spontaneous breathing activity and compliance
Pulmonary gas exchange (HM)	Inspired gas composition	PCI: the inputs influence the gas composition in the bellows representing the alveolar space, and the computer controlled uptake and delivery of respiratory and anesthetic gases
Pharmocokinetics (MM)	Drug dosages	EMI: a bar-code on a syringe identifies the drug when it is injected in an IV port, and to determine the dose, the weight of injected fluid is measured on a scale at the completion of an administration, and ANI. Infusion rates: ANI only
Neuromuscular blockade (MM)	Peripheral nerve stimulator	PCI: automatic detection of the strenght and pattern of a real nerve stimulator current applied to electrodes in the ulnar nerve location on the mannequin

Model types: MM – mathematical model; HM – hybrid model. Interface types: PCI – physico-chemical input; EMI – electro-mechanical sensing of therapeutic intervention; EI – emulated interaction with therapeutic equipment on a computer screen (not used in current HPS); ANI – alpha-numerical data entry to a computer console.

interactions, a block diagram is not a meaningful representation. Moreover, the number of modeled interactions is expected to increase significantly as the current models continue to evolve, and as new models get added. By selecting a particular model column in Table 3, one can quickly identify the inputs to that model coming from other models. For example, the inputs to the systemic uptake and distribution model for the respiratory gases and volatile anesthetic agents are: 1) the blood volume and flow rates in different tissue compartments (from the cardiovascular model), and 2) the alveolar partial pressures (from the pulmonary gas exchange). Likewise, by selecting a row in Table 3, one can identify the outputs a particular model sends to other models. For example, the pharmacokinetic model outputs different effector site drug concentrations to the cardiovascular and respiratory physiologic control mechanisms and pharmacodynamics, and to the model for neuromuscular blockade.

Describing in detail the different physiologic and pharmacological models is beyond the scope of this paper. The cardiovascular [16]; systemic uptake and distribution [17–20], and pharmacokinetic models [21, 22] result from adaptations or enhancements of models published in the scientific literature. Two original mathematical models combine the physiologic control mechanisms and pharmacodynamics for the control of spontaneous breathing and circulation, respectively. The hybrid mechanical lung model, the model for neuromuscular blockade, and a parameter estimation procedure for the pharmacokinetic models were also developed specifically for the UF-METI HPS system. In the cardiovascular model, two important additional submodels can be distinguished: a mathematical model for the myocardial oxygen supply-demand ratio determines various stages of myocardial ischemia, and a cardiac rhythm model generates dysrhythmias with appropriate ECG and contractile activity depending on the level of myocardial ischemia. The systemic uptake and distribution influences the cardiovascular model through the oxygen saturation of the arterial blood and the myocardial oxygen supply model (see Table 3). The transport of intravenous drugs is accomplished using traditional second or third order pharmacokinetic models, rather

Table 2. Outputs from the mathematical and hybrid (mathematical–mechanical) models to the monitoring instruments and clinical signs of the UF-METI HPS

Model	Outputs	Interface type and implementation
Cardiovascular (MM)	Arterial, pulmonary artery and central venous blood pressures	EMO: electrical stimulation by a computer controlled analog signal of the wires going to the blood pressure monitor
	Electrocardiogram	PCO: computer controlled analog signal on electrodes attached to the patient mannequin
	Heart sounds	PCO: computer selected sounds in synchrony to the cardiac cycle played on speakers under the skin of the mannequin
	Palpable pulses	PCO: computer controlled pneumatic pulses in radial and carotid artery locations on the mannequin
Lung mechanisms (HM)	Airway pressures and flows	PCO: the outputs are generated by a pneumatic system, containing an anatomically correct upper airway, computer controlled airway resistance, and bellows representing alveolar volume with computer controlled spontaneous breathing activity and compliance
	Breath sounds	PCO: computer selected sounds in synchrony to the respiratory cycle played on speakers under the skin of the mannequin
Pulmonary gas exchange (HM)	Expired gas composition	PCO: the output is determined by the flow of gas in the upper airways, and by the gas composition in the bellows representing the alveolar space, resulting from a computer controlled uptake and delivery of respiratory and anesthetic gases
Systemic uptake and distribution (MM)	pH, $PaCO_2$, PaO_2	ANO
	SpO_2	EMO: stimulation by a pulse-oximeter probe by a device emitting two wavelenghts of infrared light
Neuromuscular blockade (MM)	Thumb movement on stimulus	PCO: computer controlled movement of the mannequin thumb by a stepper motor

Model types: MM – mathematical model; HM – hybrid model. Interface types: PCO – physico-chemical output; EMO – electrical or electro-mechanical actuation; EO – emulated monitor or vital sign on a computer screen (not used in the current HPS); ANO – alpha-numerical data display on a computer monitor. $PaCO_2$ – partial pressure of arterial carbon dioxide; PaO_2 – partial pressure of arterial oxygen; SpO_2 – oxygen saturation as measured by pulse oximetry.

than by a multi-compartment uptake and distribution type model. The major advantage of the pharmacokinetic model is that it contains fewer, more easily identifiable parameters. The disadvantage of the pharmacokinetic model is that the influence of cardiac output and blood volume have to be implemented explicitly. Work on this model is currently in progress, as indicated by the brackets in Table 3.

CONCLUSION AND PERSPECTIVE

Four levels of design decisions play an important role in the quality and success of a full-scale simulation exercise. These levels are: hardware, software, curriculum, and exercise design. The clinical instructor designing simulator based curricula and exercises must, to a certain extent, understand hardware and software design decisions made by the simulator developers. To facilitate this important communication, this paper reviews specific hardware and software design decisions, such as: the use of script-controlled and model-driven simulation engines, and the different types of interfaces and models that are used in the current full-scale simulators. To illustrate these concepts, we presented the inputs, outputs and interactions between physiologic and pharmacological models of the UF-METI HPS. By aligning design decisions at all four levels, the range of educational applications for full-scale patient simulators can be significantly widened. This understanding between

Table 3. Interactions between the mathematical and hybrid models of the UF-METI HPS

	Cardiovascular	Lung mechanisms	Pulmonary gas exchange	Systemic uptake and distribution	Pharmacokinetics	Cardiovascular PC and PD	Respiratory PC and PD	Neuromuscular blockade
Cardiovascular	×		Pulmonary blood low	Blood volume and flow in tissue	[Cardiac output, blood volume]	Mean arterial pressure		
Lung mechanics	Intrathoracic pressure	×	Gas flow rates and volumes				[Lung stress receptors]	
Pulmonary gas exchange		Net gas exchange	×	Alveolar partial pressures				
Systemic uptake and distribution	O_2 saturation of arterial blood		Central venous partial pressures	×		PO_2 in the brain	PO_2 in the arterial blood, PCO_2 in the brain	
Pharmacokinetics					×	Effector site drug concentrations	Effector site drug concentrations	Effector site drug concentrations
Cardiovascular PC and PD	Heart rate, contractility, SVR, capacitance					×		
Respiratory PC and PD		Respiratory muscle pressure					×	
Neuromuscular blockade		Respiratory muscle blockade						×

PC – mathematical model of physiologic controls; PD – mathematical model of pharmacodynamics. Planned , but not yet implemented model interactions are indicated by brackets.

clinical educators and simulator designers is a first step toward an open model architecture, which will allow clinical educator specialists to create their own physiologic or pharmacological model extensions for patient simulators.

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REFERENCES

1. Denson JS, Abrahamson S. A computer-controlled patient simulator. JAMA 1969; 208: 504–508
2. Gaba DM, DeAnda A. A comprehensive anesthesia simulation environment: re-creating the operating room for research and training. Anesthesiology 1988; 69: 387–394
3. Good ML, Gravenstein JS. Anesthesia simulators and

training devices. Int Anesthesiol Clin 1989; 27 (3): 161–168
4. Chopra V, Engbers FH, Geerts MJ et al. The Leiden anaesthesia simulator. Br J Anaesth 1994; 73: 287–292
5. Gaba DM. Simulator training in anesthesia growing rapidly, CAE model born at Stanford. J Clin Monit 1996; 12: 195–198
6. Euliano TY, Good ML. Simulator training in anesthesia growing rapidly, Loral model born in Florida. J Clin Monit 1997; J Clin Monit 1997; 13: 53–57
7. Friedman CP. Anatomy of the clinical simulation. Acad Med 1995; 70: 205–209
8. Howard SK, Gaba DM, Fish KJ, Yang G, Sarnquist FH. Anesthesia crisis resource management training: Teaching anesthesiologists to handle critical incidents. Aviat Space Environ Med 1992; 63: 763–770
9. Holzman RS, Cooper JB, Gaba DM et al. Anesthesia crisis resource management: real-life simulation training in operating room crises. J Clin Anesth 1995; 7: 675–687
10. Euliano TY, Caton D, van Meurs WL, Good ML. Modeling obstetric cardiovascular physiology on a full-scale patient simulator. J Clin Monit 1997; in press
11. Schwid HA, O'Donnell D. The Anesthesia Simulator-Recorder: A device to train and evaluate anesthesiologists' responses to critical incidents. Anesthesiology 1990; 72: 191–197
12. Schwid HA. A flight simulator for general anesthesia training. Comput Biomed Res 1987; 20: 64–75
13. van Meurs WL, Euliano TE. Model driven simulators from the clinical instructor's perspective: current status and evolving concepts. In: Henson L, Lee A, Basford A, eds. Simulators in Anesthesiology Education. New York: Plenum, 1997; in press
14. van den Bosch PPJ, van der Klauw AC. Modeling, Identification and Simulation of Dynamic Systems. Boca Raton, Florida: CRC Press, 1994
15. Beneken JEW, Rideout VC. The use of multiple models in cardiovascular system studies: transport and perturbation methods. IEEE Trans Biomed Eng 1968; 15: 281–289
16. Beneken JEW, DeWit A. A physical approach to hemodynamic aspects of the human cardiovascular system. In: Reeve EB, Guyton AC, eds. Physical Bases of Circulatory Transport: Regulation and Exchange. Philadelphia: Saunders, 1967; 1–45
17. Zwart A, Smith NT, Beneken JEW. Multiple model approach to uptake and distribution of halothane: The use of an analog computer. Comput Biomed Res 1972; 5: 228–238
18. Mapleson WW. Circulation-time models of the uptake of inhaled anaesthetics and data for quantifying them. Br J Anaesth 1973; 45: 319–334
19. Fukui Y, Smith NT. Interactions among ventilation, the circulation, and the uptake and distribution of halothane–use of a hybrid computer multiple model: I The basic model. Anesthesiology 1981; 54: 107–118
20. Eger EI II. Uptake and distribution of inhaled anesthetics. In: Miller RD, ed. Anesthesia. New York: Churchill Livingstone, 1986; 309–331
21. Hull CJ, van Beem HB, McLeod K et al. A pharmacodynamic model for pancuronium. Br J Anaesth 1978; 50: 1113–1123
22. Sheiner LB, Stanski DR, Vozeh S, Miller RD, Ham J. Simultaneous modeling of pharmacokinetics and pharmacodynamics: Application to d-turbocurarine. Clin Pharmacol Ther 1979; 25: 358–371