TITLE: PHARMACOKINETIC AND PHARMACODYNAMIC MODELLING FOR ANESTHESIA SIMULATION

AUTHORS: I. Beinlich, M.D., D.M. Gaba, M.D., J.D.Williams, MSEE, W. Ebling, PhD.
AFFILIATION: Department of Anesthesia, Stanford University;

We describe a comprehensive framework to approximate pharmacokinetics and pharmacodynamics for use in the CASE anesthesia simulator[1]. The goal of this simulator is to provide a tool for anesthesia training and patient safety research using a realistic approximation of human physiology. We have chosen to model the effects of drugs as mediated through receptors. Each drug can interact with one or more receptors, which in turn can cause a number of physiologic effects. Each receptor may be affected by multiple drugs and each physiologic feature (e.g. vasoconstriction) may be affected by multiple receptors. We have implemented this model in an object-oriented, graphical environment for rapid prototyping and development *(Figure 1)*.

The model is comprised of drug, receptor, and effect objects which can be linked dynamically. Each *drug* owns a pharmacokinetic model which tracks bolus doses and infusion rates to compute the drug concentration in the blood and a hypothetical "effect compartment." Each drug is linked to one or more receptors through a *receptor-kinetic* which converts the drug level to a fraction of its binding constant (Kd) at each receptor based on whether the drug is a full agonist, partial agonistic, or antagonist.

Each *receptor* then sums the Kd fractions from each of its agonists and antagonists to determine the effective total occupancy via the Michaelis-Menten equation. This receptor occupancy is then translated into a receptor *effect* which combines with other receptor effects to alter a parameter in the main cardiovascular and respiratory simulation. For simplicity we assume that occupancy-effect relationships are linear although non-linear functions are possible.

The current prototype incorporates twelve drugs (thiopental, etomidate, midazolam, diazepam, dentanyl, naloxone, norephinephrine, epinephrine, dopamine, dobutamine, phenylephrine, atropine); six receptors (alpha$_1$, beta$_1$, muscarinic, opiate, barbiturate, benzodiazepine); and six effects (venous capacitance, arterial resistance, myocardial contractility, sinus rate, atrio-ventricular conduction, and respiratory depression). To be comprehensive the model will require substantially more drugs, receptors, and effects.

This approach is unique because it links kinetics and receptor-theory to physiologic modelling. Drugs of the same class appropriately saturate their receptor; synergism between drugs of different classes can occur when multiple receptors affect a single physiologic feature.

This framework may be useful for teaching the integrated effects of drugs and reflexes in animals or humans. The model needs to be tested by expert clinicians who "administer" drugs to the system as data on receptor pharmacology and occupancy-effect relationships in man are incomplete.

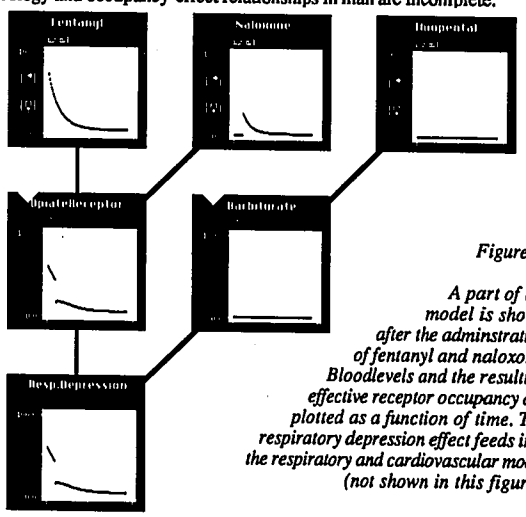

Figure 1:

A part of the model is shown after the adminstration of fentanyl and naloxone. Bloodlevels and the resulting effective receptor occupancy are plotted as a function of time. The respiratory depression effect feeds into the respiratory and cardiovascular model (not shown in this figure).

References: 1. *Anesthesiology* 69:387-394, 1988

A1042

TITLE: CORRELATION BETWEEN RESIDENT AND PEER EVALUATION OF ANESTHESIA LECTURES

AUTHOR: Murali Sivarajan, M.B.,B.S.

AFFILIATION: Kasturba Medical College, Manipal, Karnataka, India; and, Department of Anesthesiology, University of Washington School of Medicine, Seattle, WA 98195

It is common practice to evaluate teaching effectiveness by having students evaluate teachers. The reliability and validity of such evaluations have been established using only undergraduate (college) students having extended contact with teachers.[1] In our residency program, although the faculty have extended contact with residents in the clinical setting, each faculty person gives an average of only three lectures to residents each year. Assuming that faculty evaluating the lectures given by their peers would be valid, I wished to determine if there is any correlation between resident and peer evaluations in a setting in which each faculty person gives only a few lectures each year.

Method. A series of 62 lectures on anesthesia and anesthesia related topics delivered by 20 faculty anesthesiologists at a four-day course open only to anesthesia residents was evaluated by the residents (n=50) as well as the faculty (n=19). Each lecture was evaluated on three categories, namely: Quality, Content, and Usefulness to residents, on a five point scale, one being extremely poor and five being excellent. Mean scores for each category of each lecture were calculated and placed in rank-order from high to low scores. The rank-order derived from resident evaluations were compared to rank-order derived from peer evaluations using Spearman's Rank Correlation Coefficient (γ_S, see below). Also, the mean scores for each category from resident and peer evaluations were compared to each other using Student's *t*-test for unpaired observations.

Results. There were statistically significant correlations in the rank-orders of scores derived from residents and peer evaluations (see values below). There was no significant difference between the mean scores from resident evaluations and those from peer evaluations.

	Quality	Content	Usefulness
γ_S	0.57*	0.50*	0.54*

* $p < 0.001$

Conclusion. In this study, where the residents were drawn from different programs and had only limited contact with the faculty, there was good correlation between resident and peer evaluations, lending validity to the resident evaluations.

Reference.

1. Doyle et al: J Educ Psychol 70:815-826, 1978