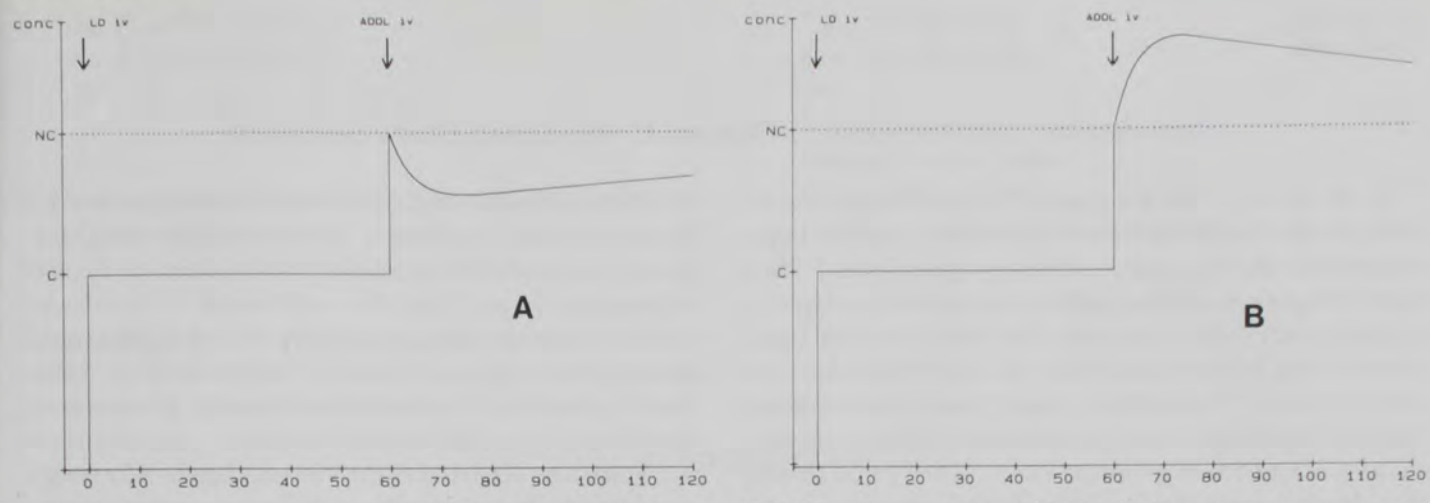

FIG. 1. A computer simulation of the predicted plasma concentration (CONC) using equation 2 of Alvis *et al.*[1] The proposed equations are adequate for the first desired concentration (C), but when a higher predicted concentration is desired (NC), an under prediction (*A*) or over prediction (*B*) from the desired level occurs, depending on the definition of "t" in equation 2.

$$u_1(t) = V_c \cdot C \cdot M_p \cdot (k_{10} + k_{12} \cdot e^{-k_{21} \cdot t} + k_{13} \cdot e^{-k_{31} \cdot t}) + V_c \cdot (NC - C) \cdot M_p \times (k_{10} + k_{12} \cdot e^{-k_{21} \cdot (t-t_1)} + k_{13} \cdot e^{-k_{31} \cdot (t-t_1)}) \quad (3)$$

where the origin of t is the time at which the *initial* loading dose was administered, and t_1 is the time at which the *first additional* loading dose is given. Similarly, although somewhat more complex, the solution can be derived for the infusion rate after the nth additional bolus, using again the superposition principle.

PIERRE MAITRE, M.D.
SAM VOZEH, M.D.
Department of Anesthesia and Division of Clinical Pharmacology
Department of Internal Medicine University of Basel / Kantonsspital CH-4031 Basel, Switzerland

DONALD STANSKI, M.D.
Associate Professor of Anesthesia Stanford University School of Medicine Veterans Administration Medical Center Palo Alto, California 94305

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In Reply:—We appreciate the insightful and thorough analysis offered by Drs. Maitre, Vozeh, and Stanski; we are continually modifying and upgrading our CACI software, and we will actively consider the relevance to our current system design of the suggestions provided. We find CACI to be a useful tool for both clinical research and patient management, and we are pleased to hear of others who share our interest in pharmacokinetically driven drug infusion.

J. MICHAEL ALVIS, M.S.
JAMES R. JACOBS, B.E.S.
J. G. REVES, M.D.
Department of Anesthesiology Duke University Medical Center Durham, North Carolina 27710

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