



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 n th additional bolus, using again the superposition principle.

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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.

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