Anesthesiology
2000; 92:628

In Reply:—We thank Dr. Rampil for bringing up the matter of experiment design. Although in some circumstances system identification using a single fixed-size step change input may indeed suffer from the limitations described, our approach is very close to optimal. In our study,[1] we applied one or more steps in and out of end-tidal anesthetic concentration of variable duration depending on the observed dynamics of the bispectral index (BIS; see fig. 3).

When there is no information available on applicable model structures, a pseudorandom binary sequence can be a useful test signal, but the choice of length and switching interval need to be guided by step-response data.[2] However, when information on applicable model structures is available, it can be used to design more optimal test signals.[2,3]

With the anesthetic literature in mind, it is reasonable to assume a nonlinear relation between effect-site concentration and electroencephalographic (EEG) effect parameter and that there is a lag between end-tidal concentration and effect that is mainly determined by the blood-brain tissue partition coefficient. The nonlinear relation can be identified from step-response data because the effect-site concentration does not change in a stepwise fashion.

For the proposed model and the estimated population parameters, and taking into account the experimental conditions, we constructed *a posteriori* an optimal binary sequence by maximizing the determinant of the information matrix.[3] The information gained by using the optimal input signal (which deviated only minimally from step inputs) instead of the optimal single-step signal is negligible in the light of interindividual variability and the fact that step durations depended on the occurrence of near steady states in measured bispectral index (BIS) values. It is of interest to note that for a nonlinear model of the ventilatory controller consisting of a slow and a fast compartment, Bellville *et al.*[4] found that step changes provided the most information on the values of the model parameters.

Erik Olofsen, M.Sc.
E.Olofsen@Anesthesiology.MedFac.LeidenUniv.nl
Albert Dahan, M.D., Ph.D.
Department of Anesthesiology
Leiden University Medical Center
The Netherlands

References

1. Olofsen E, Dahan A: The dynamic relationship between end-tidal sevoflurane and isoflurane concentrations and bispectral index and spectral edge frequency of the electroencephalogram. ANESTHESIOLOGY 1999; 90:1345–53

2. Godfrey K: Introduction to perturbation signals for time-domain system identification, Perturbation signals for system identification. Edited by Godfrey K. New York, Prentice Hall, 1993, pp 1–59

3. Goodwin GC, Payne RL: Dynamic system identification. New York, Academic Press, 1977

4. Bellville JW, Ward DS, Wiberg D. Respiratory system. Modelling and Identification, Systems and Control Encyclopedia: Theory, Technology, Applications. Edited by Singh HG. Oxford, Pergamon Press, 1988, pp 4055–62

(Accepted for publication September 23, 1999.)

Anesthesiology
2000; 92:628–9

Chemical Skinning Artifact Appears to Increase Sensitivity of Masseter Muscle to Halothane and Succinylcholine

To the Editor:—The distinguished laboratory at Lille, France, has reported undue sensitivity to halothane[1] and caffeine[2] in fragments of human masseter muscle that have been chemically skinned and exposed to these agents at temperatures less than 37°C. Reyford *et al.*[1] conclude that this may help to explain causes of masseter spasm in humans who receive halothane and succinylcholine; however, Melton *et al.*[3,4] have contradictory evidence regarding masseter responses. Biopsies of human masseter muscle were taken during complex facial and skull-base surgery, and the dissected bundles were exposed to halothane or caffeine at 37°C using the North American malignant hyperthermia testing protocol.[3,4] These bundles were not sensitive to either agent; only two bundles (40- and 50-mg tension) had a contracture after 3% halothane. Furthermore, the mean caffeine concentration producing a 0.2-g increase was 5.5 mM; one caffeine bundle increased tension at 2 mM, but only to 35 mg. Although calcium release in skinned masseter muscle is different from that of skinned vastus when exposed to these drugs, this difference may not directly apply to responses *in vivo*. We suggest that chemical skinning, perhaps related to use of fragments, may be responsible for this apparent discrepancy. Although the bundle weight in our study was less than that in the usual biopsy, twitch amplitude was excellent. Therefore, our *in vitro* results[3,4] may