ON A MATHEMATICAL THEORY OF QUANTAL RESPONSE ASSAYS

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1. Introduction

About seven years ago, one of the authors (Puri [16]) was confronted with the following biological phenomenon. At time $t = 0$, each member of a group of hosts such as animals is injected with a dose of a specified virulent organism such as viruses or bacteria, which elicit a characteristic response from the host during the course of time. This response may be death, development of a tumor, or some other detectable symptom. If $n(t)$ denotes the number of hosts not responding by time t, the plot against t of either $n(t)$ itself or of the proportion $n(t)/n(0)$ is known as the time dependent response curve. These response curves differ with the dose and with the type of the organism. However, generally speaking, the larger the injected dose, the sooner the host responds. The question was raised as to how one could explain these observed response curves through a suitable stochastic model. Upon a search of the existing literature at the time, it was found that most of the models considered until then, were based on the hypothesis of existence of a fixed threshold, namely, while the organisms are undergoing certain growth processes within the host, as soon as their number touches a fixed threshold N, the host responds. In [16], this hypothesis was abandoned; first, because this hypothesis is not strictly correct; second, it is not clear what value one ought to choose for N in a given situation, and third, because this hypothesis makes the algebra unnecessarily intractable due to the involvement of the first passage time problem. Instead an alternative hypothesis originally suggested by Professor Lucien LeCam was adopted. Here, unlike in the threshold hypothesis, the connection between the number $Z(t)$ of organisms in a host at time t and the host's response is indeterministic in character. More exactly, it is assumed that the value of $Z(t)$ (or possibly of a random variable whose distribution is dependent on the process $\{Z(t)\}$) determines not the presence or the absence of response, but only the probability of response of the host. Mathematically, this amounts to postulating the existence of a nonnegative risk function $f(x, t)$ such that

The work of Prem S. Puri was supported in part by the U.S. Public Health Service, N.I.H. Grant GM-10525, at the Statistical Laboratory, University of California, Berkeley. The work of Jerome Senturia was supported by the National Science Foundation Traineeship Grant 3392-80-1399 at Purdue University.