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STATISTICAL MODELS FOR THE ACTION OF DRUGS

The action of even a single drug upon a biological organism involves, in general, a complex sequence of processes, and if more than one drug is present, the situation is further complicated. The role of mathematical models in this context is widely recognized, and such models are essential if the dose-response relationship is to be described in quantitative terms.

In this paper a general framework is established for the representation of the action of drugs when applied alone or in combination with other drugs. This framework is then employed to construct a system of models for the action of drugs on physiological systems in human subjects. The approach is, however, capable of application to a wide range of phenomena, and for this reason a general structure and general terminology have been adopted. All three basic concepts, the stimulus (and its components). the system (and its subsystems) and the site of action, are well established. The classification of joint action models is presented: independent joint action, interactive joint action, synergism and antagonism, similar joint action.

A system of models based on a simplified view of the action of drugs upon the central nervous system is considered. These models involves a specific representation of the processes taking place at the sites of action. We suppose that the sites of action correspond to clusters of synapses. The framework of these models involves three main concepts: the number of components of the stimulus, the number of subsystems and the number of sites of action. The various combinations of the alternative values are developed in detail. The models described cover a wide variety of forms of joint action, and the inclusion of more than two sites of action and more than two subsystems offers the opportunity of extending the scope of the models still further.

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