Models of agonist–antagonist interaction

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Competitive agonist-antagonist interactions are studied using the Schild equation (Arunlakshana & Schild, 1959). Recently, this has been modified to include the so-called 'co-operative' models of drug-receptor interaction, (Colquhoun, 1973). Geometry can be used to display these relationships and give pictures in three dimensions which yield more information that their equivalent equations. For example, the Schild equation is seen to be that of a hyperbolic paraboloid. Symmetries can then easily be discovered which reveal new designs for experiments. These designs make it possible to cover the range of available data in ways which are best, both in terms of unbiased exploration and of experimental economy.

The demonstration consists of physical models and drawings on isometric graph networks (Figure 1).

Usually competitive antagonism is evidenced by parallel shift of a dose-response curve or a linear plot when the dose ratio of the Schild equation is plotted against the antagonist dose. This can be established with equal rigour, greater economy and better statistical freedom by using the vector equations

$$\cos \gamma = \frac{y \cdot x}{|y||x|} = \frac{z \cdot x}{|z||x|}$$

$|y| = |z|$, and the symmetries shown in Figure 1 about the central parabola of the system,

$$X(t) = (t-1, \; t^2, \; t),$$

where t is a parameter.
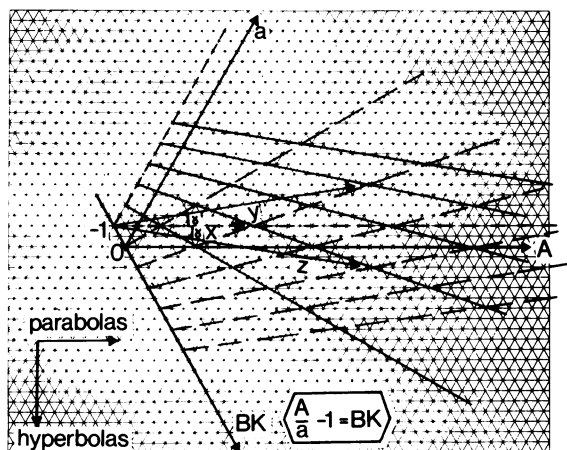
Figure 1 The Schild equation plotted on isometric paper. A is the agonist dose in presence of antagonist at dose B. The equieffective dose of agonist alone is a; K is the antagonist affinity constant. X, Y, Z are vectors, y is the angle between them.

References

ARUNLAKSHANA, O. & SCHILD, H.O. (1959). Some quantitative uses of drug antagonists. *Br. J. Pharmacol.,* **14,** 48–58.

COLQUHOUN, D. (1973). Classical and co-operative models for drug action. Proceedings of a Biological Council Symposium in Drug Receptors, Ed. Rang, H.P., London: Macmillan, pp. 149–182.