native models, and selection of the "best model" on the basis of objective criteria.

- It permits simultaneous analysis of data from multiple curves or multiple experiments.

- It can provide tests of similarity of shape of two binding isotherms, and enable one to estimate the relative scaling factors for two or more binding isotherms of similar shape.

In summary, the Scatchard plot is no more and no less subject to abuse than other plots which in fact have the same informational content. Graphical methods serve well to provide subjective, preliminary understanding of the data. However, such methods sometimes oversimplify, with the paradoxical result that different graphs of the same data appear to lead to different conclusions. Such paradoxes are usually resolved with the use of an appropriate statistical analysis.

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References and Notes


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Munson and Rodbard (1) present in summary their views of the difficulties encountered in analyzing ligand-receptor interactions. Most of their presentation is perfectly acceptable and analyzes issues not touched upon in my report (2), but there are some misleading statements to which I take exception.

If a set of algebraic equations can be transformed into each other, then the "statistical information content of the data" is indeed the same in terms of any one of them. Graphs, however, make their impact by a visual interaction with the observer, and they can distort in different ways the implications of a set of data. Thus some graphs can lure one into false conclusions. For example, Fig. 1 shows the same data plotted in two different coordinate systems. In each figure a tenfold change in concentration of free ligand, F, is represented by a bar, I or I, of appropriate length. It is immediately obvious that at increasing F there is an enormous compression of information in the top (Scatchard) graph, but a uniform distribution in the B-log F coordinate system. It is for this reason that I pointed out previously (2) that the former graph is more deceptive than the latter in leading people to believe that B_max can be established by extrapolation. For both cases, however, I also stated explicitly that "unless reliable binding data can be obtained at [high] ligand concentrations ... any [graphical] estimate of B_max will be uncertain."

It would also be desirable to distinguish between a "Scatchard graph" and a "Scatchard analysis." The latter may be used with no graph or with any graph. Scatchard analysis refers to a particular algebraic format for analyzing binding data, and depends on the assumption of a very restrictive molecular model for the receptor system. One obtains the impression from Munson and Rodbard (1) that an algebraic analysis of binding data must begin "with a particular model." That is not true. It has long been known (3-5) that a binding equation in terms of stoichiometric equilibrium constants is valid broadly, for homogeneous noninteracting sites, for two, three, or more classes of independent sites, when there is positive cooperativity between sites, when there is negative cooperativity, when there is positive and negative cooperativity, and so forth. Furthermore, from principles of algebra it has been shown that the stoichiometric binding equation can be transformed into a format that very deceptively looks like the Scatchard equation but is not; the binding constants of the former are for an ensemble of imaginary, isolated, ghost sites, and, except in very special circumstances, do not correspond to those of real sites. Thereafter, if a model is assumed, binding constants for the real sites may be extracted. If one uses this mathematical procedure, one recognizes that a particular model is only one solution to the general binding equation, which may or may not be in accord with knowledge of molecular structure (5).

It may be, as Munson and Rodbard state (I), that the "biologist . . . does not use K . . . and B_max in the same sense . . . as the enzymologist or physical chemist." If so, it behooves such biologists to define new symbols and new names for their new and different quantities, or confusion will be propagated in the literature.

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