effects are suitable for this purpose, though they may be interesting for other reasons; and not all sublethal toxic effects have any particularly clear ecological significance. They may, in fact, be quite trivial.

4.6 Quantitative Structure-Activity Relationships (QSARs)

In Section 4.2.1 it was seen that in a homologous series of linear alkylate sulphonate detergents, a regular empirical relationship could be discerned between the lethal toxicity of the detergent and the length of the hydrocarbon chain. This is a simple example of a *quantitative structure-activity relationship,* or QSAR. To determine whether or not a QSAR exists for a particular group of chemicals, it is necessary to plot a graph to show the relationship between some measure of biological activity (such as 96-h LC50, bioconcentration factor, or the concentration causing some sublethal effect) against some structural parameter (chain length, molecular weight) or some value closely related to structural parameters such as octanol-water partition coefficient. If a good correlation is found, using univariate or multivariate linear or non-linear regression techniques, the QSAR for this group of chemicals can be a useful predictive tool.

For example, if measured toxicity data for several of a particular group of chemicals are available, it becomes possible to predict with reasonable accuracy the likely toxicity of any other chemical in the group. This can afford considerable savings of time and resources in the development of novel compounds, or where a chemical is encountered for which no data on biological activity are available. Another possibility is that of predicting the toxicity of chemicals to one species based on data for another species. This situation commonly arises, since the bulk of the available data relates to a relatively small number of 'standard' species, whereas the species under threat from real pollution incidents are usually of another kind. Figure 4.20 shows the basis of this idea. The line is based on the open circles, which are coordinates of a plot of the toxicity of 16 chemicals to *Daphnia* against the toxicity of the same chemicals to the guppy. Note that this line is *not* a QSAR. Superimposed on this line are toxicity *predictions* based upon the QSAR for this group of chemicals for *Daphnia*. The fact that all the data points, whether real or predicted, fall close to the line suggests that for this group of chemicals, the two species share a common QSAR. This does not mean that the toxicity of the chemicals to the two species is the same. However, it does mean that the *Daphnia* QSAR can be easily adapted to make predictions for this group of chemicals against the guppy. In principle, it should then be necessary only to undertake real tests on a new species with a few chemicals in a series, to establish the commonality of the QSAR, in order to be able to make reasonable estimates of toxicity of the whole group to that species (Lloyd, 1991b).

There are still, however, some limitations on the use of QSARs which

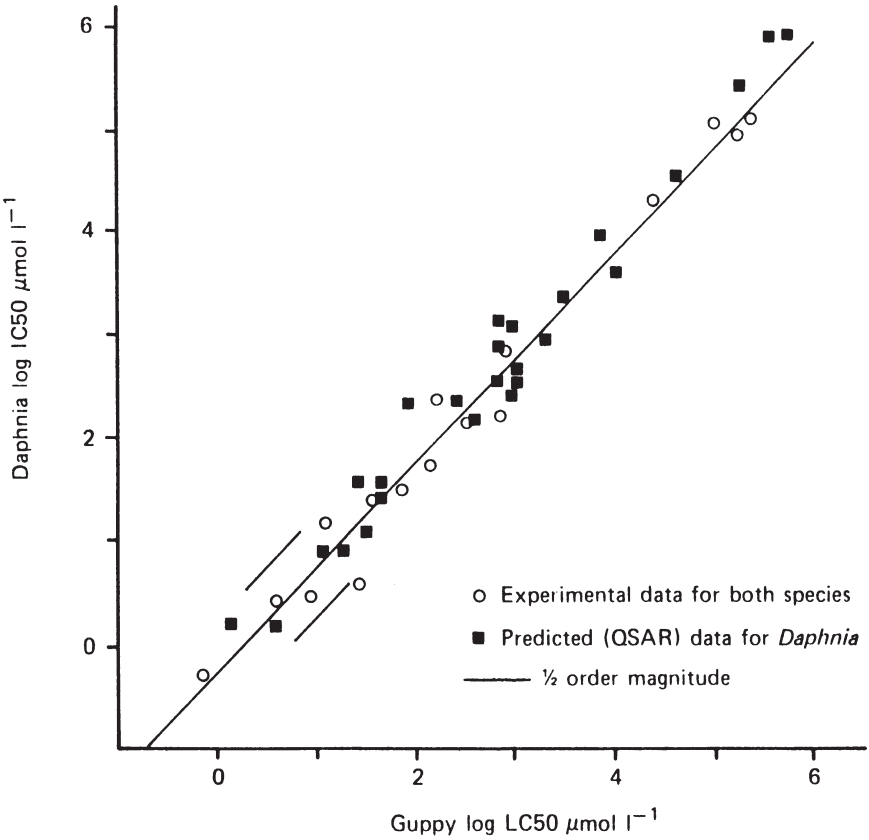

Figure 4.20 Correlation between the sensitivities of two organisms to 42 industrial organic chemicals. After Lloyd (1991)

means that they cannot yet be considered a substitute for real measurements in risk assessment, but rather as a useful aid. First, QSARs are correlations, not causal relationships. In any group of chemicals, it is not uncommon to find one or more which cause the QSAR to break down. There are several possible reasons for this, but one important one is that the idea of QSARs makes a hidden assumption, that each chemical in the QSAR has basically the same mechanism of action in the living organism. This is not necessarily the case. However, where it can safely be assumed that a group of chemicals does have the same mechanism of action, a further possibility is opened that a group of chemicals in a QSAR do not have to form a homologous series, or be structural isomers, or necessarily to have any such close chemical similarity. Thus the idea of QSARs could be extended to very large groups of chemicals indeed. Of course, the term 'mechanism of action' subsumes a complex series of biological and chemical processes, but some attempt has been made to recognise basic modes of action in terms of the symptoms poisons

produce in fish: so-called *fish acute toxicity syndromes* (FATS). Five toxic syndromes have been recognised so far (Lloyd, 1991b): respiratory uncoupling, respiratory irritation, acetylcholinesterase inhibition, and narcosis types I and II. Any chemical which causes one of these syndromes at acutely-toxic levels in fish appears to form a QSAR with all others which cause the same syndrome. This empirical finding appears greatly to extend the potential of QSARs in the future.

Second, QSARs do not appear to work well with chemicals which are strongly polar; they work best with non-polar organic chemicals. QSAR predictions are also insufficiently accurate for many purposes—in view of the many factors which can influence a measurement of toxicity, predictions to within an order of magnitude are probably the best that can be achieved. Nevertheless use of QSARs is a promising approach which at the very least offers the possibility of a substantial reduction in the number of toxicological experiments which currently need to be carried out. Konemann (1981) and Kaiser (1987) are useful sources of further information.