threshold dose exists. This paradox can now be understood in the framework of the above discussion. Thus the 3,4-oxide of bromobenzene reacts in an S_N2 fashion, that is, selectively with strong nucleophiles such as glutathione. Only when body glutathione is depleted by reaction with an equivalent of bromobenzene oxide will this oxide react in appreciable quantity with the next most nucleophilic groups, which are on proteins. The toxicity arises as a result of this covalent reaction with proteins[29]. DNA, a poor nucleophile, is presumably not attacked in the presence of proteins. On the other hand, I have described here how the arene oxide (I) from aromatic hydrocarbons can react as a carbonium ion with DNA, in the presence of glutathione and proteins, and thus no threshold need exist.

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Received April 21; accepted May 19, 1975.

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Alternatives to the use of tabulated values of distributions in statistical programmes

SPECIFIC values from tables of statistical distributions that vary with degrees of freedom and probability (for example Student's t, χ^2, correlation (r) or variance ratio (F)) are often included as input data, even to large detailed statistical packages[1,2]. Alternatively, the complete tables are held in store. The former makes the program less flexible while the latter uses store inefficiency and is impractical for desk-top computers. A common alternative practice is to use approximate values; thus for example it has been suggested[3] that for a sample number of thirty and more the values of t should be 2.0 when the probability (P) is 0.05. This value for $t(30\text{–}\infty)$ is within $\pm 2\%$ of the true value and was considered 'a close approximation [suitable] for most purposes'.

The alternative I propose is that simple equations should be formulated to calculate values for such statistical distributions to conserve store space and to make programs more adaptable. The equations should be relatively simple and within the present capabilities of small fixed-function desk-top computers.

As an example, the equation (1) is proposed as a simple approximate solution of Student's distribution of t. It was obtained by a trial and error fitting of the best equation-type and curve to a graph of the distribution data. In this equation t_{Pn} is the value of t when the probability is P, for example 0.05, and the sample number is n, thus:

$$t_{Pn} = [\exp(k_P/(n-1))] + tP_\infty - 1.0 \quad (1)$$

in which the distribution of $t_{P\infty}$ is given by:

$$t_{P\infty} = -0.1093\,(\log_{10}(1/P))^2 + 1.26\,\log_{10}(1/P) + 0.4941 \quad (2)$$

The equation giving the values of k_P used to obtain optimum values of t in equation (1) over the range of probability 0.001–0.1 and using the values of $t_{P\infty}$ from equation (2) is given by:

$$k_P = [2.7497\,\log_{10}(1.0/P)] - 1.1994 \quad (3)$$

This formula (1) provides values of t to within $\pm 5\%$ of the true value[4] for a sample number of between three and infinity and within the range of probabilities $P = 0.1\text{–}0.005$; values of t for a sample number of thirty and over are within $\pm 1\%$ of the true t. Values of t over the wider probability range of $P = 0.2\text{–}0.001$ were within $\pm 8\%$ of the true t for sample numbers of four to infinity; sample numbers over 30 were within $\pm 3\%$ of the true t.

I realise that when the confidence or fiducial limits thus obtained do not show a clear decision the true tables must be consulted or the equation suggested must be refined; but in most cases these small errors are of little consequence.

The correlation coefficient, r, can also be calculated knowing t for n pairs of samples at the probability P using the equation below (modified from Fisher and Yates[5]):

$$r^2 = t^2/[(n-2) + t^2] \quad (4)$$

Answers to statistical problems are usually presented in terms of a few standard values of probability, for example the t test confidence intervals. An iterative process could be used with suitable formulae to express the differences between sets of samples in the form of an exact probability, for example $P = 0.06$. With the present formula, results are only reliable within the range of probability 0.1 to 0.005. The use of an approximate formula to calculate the critical values of F could then result in a matrix of probabilities for a comparison of several sets of data. With desk-top computers, the latter step will depend on the demand to make statistical distributions available as fixed functions.

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Received April 16; accepted May 15, 1975.

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Erratum

In the article "Binding of flexible ligands to macromolecules" by A. S. V. Burgen, G. C. K. Roberts and J. Feeney (*Nature*, **253**, 753; 1975), the equation at the foot of the first column on page 754 should read.

$$\Delta F_1 = -RT\ln K_1 = \Delta H_1 - T(\Delta S_{tr} + \Delta S_{rot} + \Delta S_{conf.\ 1})$$

and not as printed.