Searching for cancer drugs by computer

A CDC 6600 taught to recognize patterns can pick the likely ones from the duds

Chemistry knows more than two million different compounds. Chemists often need to sort a large number of compounds according to whether or not they possess a given property. To give a simple example, it may be desirable to know which of several hundred compounds react as acids and which as bases. Such a property may depend not on one but on several characteristics of the compound, and the way in which it depends on them may not be precisely known. Calculation is rendered difficult or impossible, and much trial-and-error experiment may be necessary.

At the Lawrence Livermore Laboratory two chemists, Bruce Kowalski of the University of Washington and Charles Bender of LLL, have been working on a technique of getting computers to teach themselves how to solve such problems (SN: 9/9/72, p. 168). The most recent experiments indicate that the technique may be useful in finding cancer drugs.

The technique is based on pattern recognition. Computers are much better at recognizing patterns than human minds. A human being can see patterns at most three dimensions. A computer can recognize them in dozens of dimensions, and this is crucial to the technique since each different kind of input data adds a dimension to the pattern.

What the computer does is to look for patterns among the input data that are related to the desired output and classify the compounds according to whether or not they have the desired quality. In the process it uses feedback techniques to eliminate input data that are redundant or irrelevant to the desired output. To find someone's telephone number the seeker must know the name and address. An experimenter ignorant of the principles on which telephone directories are compiled might add other possible identifying characteristics, for example, that the person grew dahlias for a hobby. The computer would throw out the superfluous information.

In the cancer case, 200 compounds, purine and pyrimidine nucleoside derivatives, were screened for possible tumor-inhibiting properties. Some 50 molecular characteristics of these drugs were chosen as possibly related to tumor inhibition. All these drugs had been tested in animal experiments under the auspices of the National Cancer Institute. What the computer was doing was testing its technique against the laboratory results. The standard test uses the condition CA 755 (adenocarcinoma), and drugs considered eligible for further testing are those that cause a 70-percent weight reduction in solid tumors. The computer had to sort out the eligibles from the ineligibles by their molecular charcteristics alone.

First the computer eliminated 30 of the 50 structural characteristics of the molecules that had been fed to it, and then ranked the others according to their contribution to the result (an important piece of information in itself). The most important characteristic was the number of sulfur atoms per total number of atoms; the second was the number of single carbon-sulfur bonds per number of carbon atoms.

It took approximately five minutes to process the 200 drugs on a CDC 6600 computer. The computer was 94.2 percent accurate in placing drugs in the positive category (more than 70-percent reduction in tumor weight) and 92.9 percent accurate in placing them in the negative, for an overall accuracy of 93.5 percent. Results are published in the Feb. 6 JOURNAL OF THE AMERICAN CHEMICAL SOCIETY.

The technique is readily adaptable to other drugs, and it has screened drugs with comparable success under NCI's L 1210 (leukemia) and Walker 256 (solid tumor) systems. The technique's success will not do away with the need for animal (and later human) testing, but it can be used to spot promising drugs in advance and thus save a lot of work. Another possible application is tailoring compounds. Knowing what molecular characteristics are most important for a desired property may make it possible to design a drug for a particular therapy. ☐

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Kowalski and Bender watch as computer sorts possible anticancer drugs.