lysosomes and peroxisomes, each in highly purified fractions, required the more refined means of centrifugation which resulted from theoretical considerations and technical advances by de Duve and his colleagues, mainly Berthet and Beaufay. In 1969—by which time de Duve had established a flourishing Department of Biochemical Cytology at the Rockefeller University while continuing to lead his Department in Louvain as well—he organized a meeting which was sponsored by the New York Academy of Sciences on the various roles of peroxisomes in animal and plant cells.

Early in its work the Louvain group undertook the study of "storage diseases" of man; this study was under the leadership of Géry Hers, who had collaborated with de Duve since the earlier studies on insulin and glucagon. *Lysosomes and Storage Diseases*,† edited by Hers and François van Hoof and published in 1973, describes some 30 diseases, characterized by deficiencies of single lysosomal enzymes.

In recent years Christian de Duve turned his attention increasingly to lysosomes in cell pathology and disease and to lysosomes as targets for drugs. He refers to drugs acting via their effects upon lysosomes as "lysosomotropic." One of his groups in Louvain, led by André Trouet, has already obtained encouraging results in cancer chemotherapy. This group complexed the antibiotic, Daunomycin, with DNA and thus reduced its toxicity. Pinocytosis brought the complex into the lysosomes of the cancer cells, and the hydrolases removed the DNA and released the active antibiotic. In de Duve's laboratory at Rockefeller University interesting findings have been made on atherosclerosis. These suggest that abnormal lipid accumulations in aortic smooth muscle cells result from a relative deficiency in acid lipases that hydrolyze esters with long-chain fatty acids.

Rarely has a domain of cell biology or cell pathology been influenced so profoundly by a single intellect as has the lysosome-peroxisome field.

Last year an attractive book appeared which described the new International Institute of Cellular and Molecular Pathology organized by de Duve and his Louvain colleagues and just constructed in the outskirts of Brussels. On its first page is reproduced the title page of the great 1862 classic by Rudolf Virchow, "Die CELLULARPATHOLOGIE in ihrer Begründung auf physiologische und pathologische Gewebelehre." De Duve concludes the introduction in these words: "No longer held back by the impassible boundaries of the cellular world, medical research can now gain full entrance to the cell, if it allows itself to be guided by modern cellular and molecular biology. The latter disciplines, in turn, have the duty of providing medicine with the means of accomplishing this objective."

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† Academic Press, New York, 1973.

Analysis of Algorithms: Coping with Hard Problems

Although today's computers can perform as many as 1 million operations per second, there are many problems that are still too large to be solved in a straightforward manner. Even with improved solution methods, or algorithms, exact solutions to a wide range of practical problems, from routing of phone calls to scheduling of airplanes, require weeks or months of computer time and are, in effect, not feasible to obtain. Hence the investigation of still more efficient algorithms is of interest to large companies as well as to computer scientists.

The task of finding good ways to solve a large group of important problems has recently, in theory, been simplified. It was shown that many such problems are computationally equivalent, so that a solution for one of them can be used to solve the rest. For example, the problem of determining the best way to schedule events can be converted into the problem of finding the best way to store objects in the minimum amount of space. However, these equivalent problems have so far defied all attempts to solve them without using inordinate amounts of computer time. Since these problems are of great practical importance, many investigators are now devising ways to approximate their solutions and, in some cases, are showing how close certain approximations come to optimum solutions to a problem.

In their search for a good algorithm, computer scientists try to avoid those algorithms in which the number of computational steps (or the amount of computer time) is an exponential function of the size of the problem. (The size of a problem is essentially the number of bits of information required as input for the problem.) Since exponential functions increase very quickly as the size of the problem grows, such algorithms are said to be "inefficient."

The ideal algorithm is one in which the number of computational steps increases only as a polynomial function of the size of the problem. Such algorithms are said to be "efficient." The difference between an efficient and an inefficient algorithm can be dramatic. For example, one algorithm for a problem of size n might require n^2 steps (a polynomial function) while another might require 2^n steps (an exponential function. When n is increased from 10 to 20, the number of steps of an algorithm that requires n^2 steps will quadruple, whereas the number of steps of an algorithm that requires 2^n steps will increase more than 1000-fold.

A few years ago, Stephen Cook of the University of Toronto analyzed several difficult problems for which no efficient algorithms are known. He showed that all these problems are computationally equivalent in that an efficient algorithm for one of them, if it exists, could be used to solve them all. Richard Karp of the University of California at Berkeley then extended the list of equivalent problems to include many examples in such fields as network optimization, graph theory, and scheduling. Computer scientists decided to call these problems NP-complete. (The symbol NP stands for nondeterministic polynomial time. Complete indicates that a solution to one problem could be applied to all others in the set.)

No one has yet proved that efficient algorithms exist for the NP-complete problems. Many computer scientists consider the question of whether such algorithms exist to be the most important open question in the theory of computations. Since there is no known way to answer this question and since the NP-complete problems are of great practical interest, many computer scientists are choosing to work around the question by finding ways to live with the important problems that are NP-complete. In many practical applications, a special case of an NP-complete problem must be solved. The study of what makes a problem NP-complete can enable computer scientists to recognize when a special aspect of a problem is so restricted that it is no longer NP-complete.

Graph coloring problems are among several kinds of problems that have been recently analyzed to see what features make them NP-complete. According to Donald Knuth of Stanford University, such problems are often used to represent the scheduling of mutually exclusive events. For example, in scheduling classes at a university, a chemistry lecture cannot be scheduled at the same time as its laboratory. In order to represent such a scheduling as a graph coloring problem, each event is denoted by a point. When two events cannot occur at the same time, the points are connected by a line. This collection of points and lines is called a graph. Different times are denoted by different colors. The scheduling problem is then transformed into the problem of deciding whether it is possible to assign all of the different colors to the points of the graph so that no two points connected by a line are assigned the same color. The aim is to find an algorithm to solve this problem without trying out all possible color combinations, since such an algorithm would be inefficient.

Karp showed that graph coloring is NP-complete, but he did not make an analysis as to whether simplified versions of these problems might be solvable by efficient algorithms. Now Larry Stockmeyer of the IBM Research Center, Yorktown Heights, New York, has shown that graph coloring problems in which the number of colors is as small as three and the graph is planar are still NP-complete. Thus even when these problems are greatly simplified, they remain NP-complete. In fact, graph coloring problems are intrinsically so difficult that even the problem of approximating their solution to within a factor of 2 is not any easier than the original problem, according to Michael Garey and David Johnson of Bell Laboratories in Murray Hill, New Jersey.

Another approach to dealing with problems from the set NP is to devise approximate solutions to these problems and then to analyze how close the approximate solutions come to optimal solutions to the problems. Approximate solutions and their analyses have recently been reported for several important problems, including the bin packing problem and the traveling salesman problem.

Approximate Algorithms

In the bin packing problem, n objects are to be packed into the minimum number of bins. Each object takes up a certain amount of space in a bin, and each bin has a certain capacity. For example, the bins could be 1-minute commercial slots on television and the objects could be commercials, each of which takes no more than 1 minute.

Johnson and his associates have recently devised and analyzed two approximate algorithms for this problem: the first-fit algorithm and the best-fit algorithm. In the first-fit algorithm, each object is placed, in succession, into the first bin in which it fits. In the best-fit algorithm, each object is placed, in succession, in the most nearly full bin in which it fits. Johnson and his associates showed that, for either algorithm, no more than $[(17/10)L^*] + 2$ bins are used, where L^* is the smallest possible number of bins in which the numbers will fit. Moreover, they showed that if the objects are first listed in decreasing order of size before being assigned to bins, neither algorithm will require more than $[(11/9)L^*] + 4$ bins. Thus the approximate number of bins is always within about 22 percent of the optimum number.

Daniel Rosencrantz, Richard Stearns, and Philip Lewis of General Electric Corporate Research and Development in Schenectady, New York, have recently analyzed approximate algorithms for the traveling salesman problem. This problem, which occurs in many practical situations, involves finding a tour of n cities in which each city is visited at least once and the tour is of the minimum possible length. The traveling salesman problem occurs often in industrial applications, where the cities represent tasks to be done by a machine and the time between cities represents the time it takes to go from one task to the next. The shortest tour of the cities represents the order for performing the tasks that allow all of the tasks to be performed in the shortest possible time.

Various approximation methods for solving the traveling salesman problem are used in practice and often successfully. Rosencrantz and his colleagues compared these approximations to optimal solutions. For one approximate algorithm, the nearest neighbor method, they found that the ratio of the obtained tour to the optimal tour increases logarithmically with the number of cities. For another approximation method, the nearest insertion method, the ratio approaches 2 as the number of cities increases.

Both Johnson and his colleagues and Rosencrantz and his colleagues compared approximate solutions to optimal solutions in the worst case. While such techniques give bounds on how bad the approximate solutions may be, it has been experimentally observed that the average problem may not represent the worst case. Certain algorithms that are commonly used in practice are seldom foiled except by problems purposely designed to make them look bad. Ronald Graham of Bell Laboratories in Murray Hill suggests that analyses of algorithms in terms of average cases could be quite useful, but neither he nor others are yet able to define an average case.

One approach to this problem was taken by Rosencrantz and his associates who tried out approximate algorithms on what they considered to be random traveling salesman problems. They found that, for these random problems, the nearest insertion approximation was much better than the nearest neighbor approximation. In this instance then, the algorithm that performed better in the worst case also performed better in the randomly chosen case.

Although there are as yet no efficient algorithms for any NP-complete problem, progress is being made in finding and analyzing approximate algorithms. The discovery that NP-complete problems are computationally equivalent has enabled investigators to recognize these difficult problems when confronted with them. Now, when asked to solve an NP-complete problem, most computer scientists seek the best probable approximate algorithm rather than attempting what may be the impossible task of finding an efficient algorithm for an exact solution.—GINA BARI KOLATA

Additional Reading

1. A. V. Aho, J. E. Hopcroft, J. D. Ullman, *The Design and Analysis of Computer Algorithms* (Addison-Wesley, Reading, Mass., 1974).