Computer models

Cooperation on new molecules

Washington

COMPUTER models are becoming increasingly popular for designing new molecules. But all such efforts face a fundamental problem: what parameters and potential-energy equations should be used in estimating the final energy state and geometry of a novel molecule? A recently formed consortium has set itself the ambitious task of supplying those parameters and equations. A successful outcome will mean model-builders will sleep easier, confident that their new creations will behave in nature the way they do on a computer screen.

The new three-year project is headed by Biosym Technologies, Inc., a company based in San Diego specializing in software for computer-assisted molecular design (CAMD). Each year, consortium members will contribute money and manpower: $30,000 in cash support and six months of personnel time from a doctoral-level chemist. In return, consortium members have a say in the direction the project takes, as well as gaining first access to the new database and any software tools that are developed. Companies participating in the consortium are Abbot Laboratories, Cray Research, E.I. du Pont de Nemours, Merck Sharp and Dohme Research Laboratories, Monsanto, Rohm & Haas and the Upjohn Company.

For certain classes of molecules, such as polypeptides and nucleic acids, these energy functions, known as force-field functions, have been fairly well approximated. The parameters are derived not only from bond energies, but from non-bonded molecular interactions as well. Peter Kollman, professor of pharmaceutical chemistry at the University of California, San Francisco, is the author of one widely used set of these functions. But Kollman says that, when looking beyond well-characterized classes of molecules, the applicability of the force-field functions becomes uncertain.

As an example, the van der Waals forces between molecules in two classes of compounds may be similar, but the electrostatic charges may differ, forcing a model-builder to make assumptions about the best way to alter the force-field equations. The consortium hopes to develop a more generally applicable set of parameters and equations.

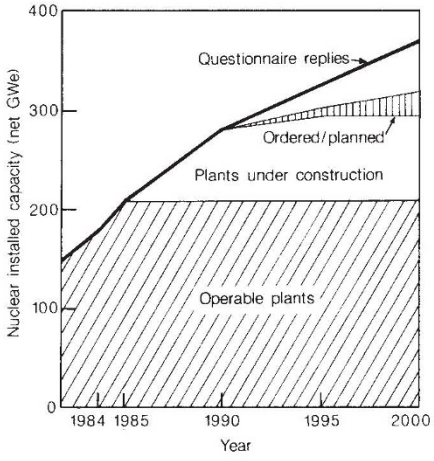
Biosym's chief scientific officer, Arnold Hagler, has also developed a well-known set of force-field equations. Hagler's plan is to use both empirical data gathered from existing literature and research done by consortium members, as well as quantum mechanics calculations, to develop a "second generation database of potential energy surfaces for organic, pharmacological and other biomolecules".

While most consortium members are also fierce competitors in the marketplace, Upjohn's director of computational chemistry, Gerry Maggiora, explains that it will be to everyone's advantage to have a good set of potential energy functions. Upjohn is heavily involved in CAMD, one focus of which is developing inhibitors of renin for use as antihypertensive agents. As the three-dimensional structure of renin has not yet been worked out, Upjohn and others have turned to related compounds such as aspartyl proteinases to study molecules that will bind to renin's active site.

John Wendoloski of du Pont says companies should probably have put more money and effort into joint developments of force-field functions in the past. Although there is nearly uniform agreement that Biosym has undertaken a potentially useful task, there are those who doubt that a general set of force-field functions can be developed at present. Cyrus Levinthal of Columbia University, who is developing a special application computer with Brookhaven National Laboratory for computing interacting forces between molecules, says it is not clear whether sufficient empirical data exist to generate appropriate parameters. That sentiment is echoed by Kollman, as well as by John McAlister, director of research for Tripos Associates, another software company also working on the force-field problem. Even consortium members confess that hoping for a "second generation" database may be optimistic, but Abbot's Jonathan Greer says a better set of parameters than those currently available will be welcome. **Joseph Palca**

Nuclear forecast

AMID Chernobyl gloom, the Nuclear Energy Agency of the Organisation for Economic Cooperation and Development (OECD) is still presenting an optimistic picture of the growth of nuclear power worldwide. In 1985, there was a 19.2 per cent increase in nuclear electricity production, the largest increase since 1977. Twenty-one per cent of electricity generated in the OECD countries comes from nuclear power stations, ahead of hydro-



thermal and geothermal (20 per cent) and oil and gas (17 per cent) but behind coal (42 per cent). Forecasts to the end of the century shown in the graph were prepared from questionnaires returned by member countries. The highest forecast includes power stations not yet at the planning stage, where worries over safety may have their effect. □

Return of tamarins proves expensive

Tokyo

THE World Wildlife Fund has agreed to an unprecedented payment of about 10 million yen ($65,000) to ensure that ten golden-headed lion tamarins illegally imported to Japan three years ago return home to Brazil, according to the Japanese Foreign Ministry. Despite the acute embarrassment the illegal import of these rare primates has brought to Japan, the Japanese government is making no move to introduce legislation to prevent a repetition of such incidents, and has failed to provide funds for the safe return of the animals.

The weakness of Japan's laws has been quickly spotted by the *yakuza*, Japan's own mafia. Just a few weeks ago, they put a black tamarin on sale on the street outside a police station at Tokyo's Shinjuku station. Their sales point, capitalizing on media attention to the smuggling of endangered species, was that the tamarin had been brought in illegally from Brazil. No action was taken against them.

The lion tamarins, trade in which is banned under the Washington Convention on International Trade in Endangered Species, to which Japan is a signatory, were brought into Japan in 1983 with false import documents (see *Nature* 318, 200; 1985). The infringement was spotted by the World Wildlife Fund's TRAFFIC office. But, having got the monkeys past customs, the importers were free from prosecution as there is no domestic legislation to back up the terms of the convention.

Only constant lobbying by the World Wildlife Fund and international protests forced the government to take action. But it has no intention of paying the bill. According to the Foreign Ministry, the monkeys will be shipped to São Paulo Zoo in mid-September at a cost of 15 million yen, two-thirds of which will be paid by the World Wildlife Fund. The remaining one-third will come from the importer and keepers of the tamarins. David Swinbanks