and two rotatable molecular bonds. Levitt and Warshel propose that the simplified representation of a protein as a set of side chains connected by virtual bonds between their α-carbon atoms is an adequate model for simulating the folding process. In other words, they propose that the computer should literally fold up a protein along the dotted lines.

The authors test this representation by simulating the folding of pancreatic trypsin inhibitor, a small protein of 58 amino acid residues and hence 57 virtual bonds. Since the most stable conformations of a molecule are those of least energy, a procedure is used which minimises the conformational energy as a function of the angles of rotation around the virtual bonds. Unfortunately, the procedure is one which does not allow the folding pathway to cross low energy barriers in the conformational energy surface, barriers which the protein in nature would be expected to negotiate readily. To avoid trapping the molecule in a conformational energy well which is surrounded by low barriers, a technique called 'normal mode thermalisation' is used after each minimisation to generate a new random starting point close to the well. The authors do not, however, allow for the possibility that during minimisation the simulated pathway of folding could be confined to a trivially shallow channel, a difficulty which could be avoided by the use of a different kind of minimisation procedure. The conformational energy surface of a protein is so complex that the use of certain traditional minimisation procedures may at worst resemble an attempt to plot the potential course of a stream by chasing a free-wheeling locomotive down a railway track. Nevertheless, the authors make the exciting point that in some of their simulations, the protein arrives at a conformation close to that of the known, biologically active structure.

One of the principal difficulties in this study is that the proposed model for a globular protein is such a drastic simplification. As a further check on the validity of their model, the authors confirm that it is apparently stable when set in the biologically active conformation. This is not, however, the sole criterion of an adequate model since the energy surface elsewhere may depart considerably from reality. Another problem is that only very few different starting conformations for the folding simulations were explored, despite the fact that folding even from the same initial conformation did not necessarily yield the same final conformation. For these reasons there still remains the danger that the approximations to the biologically active conformation obtained by simulated folding are fortuitous, and an artefact of the model and starting conformations chosen.

By far the most serious difficulty, however, is that the use of virtual bonds cannot by its very nature be a general solution to the folding problem. Neglect of the backbone with its capacity for intramolecular hydrogen bonding means that α-helical regions, and possibly other secondary structure features, lose their intrinsic stability. Possible exceptions are those helices with well defined clusters of hydrophobic or hydrophilic side chains on the helix surface, but such helices are by no means ubiquitous. It is therefore notable that Levitt and Warshel, like Ptitsyn and Rashin, were obliged to start with the known α-helical region of trypsin inhibitor in the α-helical conformation and although the virtual bonds within the helical region were allowed to vary, the helix was the part of the real protein reproduced least well after folding. As the authors point out, the various statistical pre-

The psis and their relations

from David J. Miller

SHORTLY after the discovery of the first ψ particle with a mass of 3.1 GeV/c^2 (*Phys. Rev. Lett.*, **33**, 1404 and 1406; 1974) the Berkeley–Stanford team, using the e^+e^- storage ring SPEAR at Stanford, California, found a second narrow particle with a mass of 3.7 GeV/c^2—about four times the mass of the proton (*Phys. Rev. Lett.*, **33**, 1453; 1974). The heavier particle, sometimes called the ψ' (3.7), has also been observed in e^+e^- collisions at the DORIS storage ring near Hamburg (*Phys. Lett.*, **53B**, 489; 1975). The ψ' (3.7) is narrow like the ψ (3.1). Unlike the ψ (3.1) it has not been seen in the collisions of protons, neutrons or γ rays with nuclei, but its rate of production in e^+e^- collisions is only a factor of one third down on the rate for ψ (3.1) production. The ψ' (3.7) decays to e^+e^-, to $\mu^+\mu^-$ and to many-hadron states (probably mostly pions), as does the ψ (3.1). It also decays, about 30% of the time, directly to a ψ (3.1) and two pions. No other narrow states have been reported in the mass region up to about 5 GeV/c^2, though well authenticated rumours from SPEAR tell of a broad bump in the rate of hadron production at a mass of about 4.2 GeV/c^2.

Recent issues of *Physical Review Letters* have been full of theoretical speculation about the meaning of these new objects. Most explanations fall into one of three general groups —intermediate boson models, 'charm' models or 'colour' models.

The charm or 'SU(4)' model (see *Nature*, **253**, 438; 1974, for a brief outline) is still the most popular. Various schemes have been suggested to fit the ψ and ψ' into a multiplet representation of the group SU(4). In 1961 Gell-Mann and Nishijima succeeded in explaining many of the properties of hadrons by fitting them into multiplets of SU(3)—sometimes called the 'eight-fold way' because many of the multiplets contain eight particles. If the new quantum number charm is allowed, then SU(3) can be extended into SU(4) in a very natural way—just as the previously well established SU(2) scheme of 'isotopic spin' became SU(3) when Gell-Mann added the 'strangeness' quantum number. In a simple SU(4) scheme there is an obvious place for one ψ particle, in the same multiplet as the well established vector mesons ρ, ω and φ, though it is not so easy to fit in two. If the ψ (3.1) is fitted in, then predictions have been made (by M. K. Gaillard, Rosner and others) that charmed particles called the F and the D should exist, with masses as low as 2.2 GeV/c^2. The psis could not decay into Fs or Ds, but the Fs and Ds could be produced in pairs with opposite values of the charm quantum number. It has been suggested that the bump at 4.2 GeV/c^2 may be due to the onset of F or D production, but there is no direct evidence to prove this.

A recent paper by a Toronto group (*Phys. Rev. Lett.*, **34**, 541; 1975) suggests a novel way of fitting both the ψ (3.1) and the ψ' (3.7) into the same SU(4) multiplet as the vector mesons. As well as charm, they invoke a new "medium strong" charm-breaking interaction. They assume that the ψ' (3.7) is a combination of a charmed quark and a charmed anti-quark—the obvious assignment for a ψ in the vector meson multiplet. Their new interaction allows them to make the ψ (3.1) from a different mixture of charmed and strange quarks and anti-quarks. As in other SU(4) theories, they predict other new charmed particles which should be seen soon, if they exist; if their scheme is correct the new particles should have extremely interesting properties due to the effects of the medium strong force. Perhaps this force also has something to do with the medium strong properties of the ψ (3.1) in its decay and in photoproduction (see *Nature*, **254**, 180; 1975, for a discussion of these results).