tions of the process. GARCH, or generalized ARCH models, provide a more flexible way of accounting for the persistence often observed in squared stock returns.) Interestingly, Mantegna and Stanley report that the scaling property of stock returns in the sample is not well approximated by a GARCH(1,1) model. It is possible that this would not be so if a more elaborate ARCH model were used, but their result is consistent with frequent findings that ARCH models cannot fully account for the leptokurtosis observed in high-frequency financial returns.

Changes in institutions or in the economic regime may also account, at least partially, for the observed leptokurtosis in the distribution of stock returns. Because this view allows for the possibility that large outliers in the tail of the distribution of stock returns are drawn from a different distribution than the observations in the centre, it falls well in line with the approach suggested by Mantegna and Stanley. No study so far has been able to explain the events during the market 'meltdown' of 19 October 1987 as a 'reasonable' draw from a distribution that also describes the price dynamics during more normal times. A class of Markov switching models[9] allows for time-dependence in the mixing of distributions of stock returns corresponding to different regimes. For common stock indexes there seem to be at least two regimes, one with high variance and low (negative) mean returns, and another with low variance and positive mean returns. These models can be combined with ARCH processes to provide a possibly better fit of the distribution of returns[10].

In view of the strong evidence of time-varying parameters of the distribution characterizing high-frequency stock returns, the scaling approach proposed by Mantegna and Stanley should not be regarded as a substitute for existing models such as ARCH or regime switching. Instead it is likely that the two approaches can be fruitfully combined by using the distribution suggested by Mantegna and Stanley to model the residuals from one of the classes of models which has proved successful in forecasting the volatility of stock returns. □

Allan Timmermann is in the Department of Economics, University of California at San Diego, 9500 Gilman Drive, La Jolla, California 92093-0508, USA.

OBITUARY

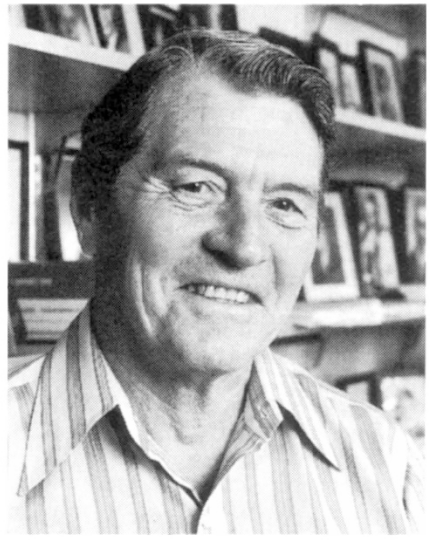
Christian B. Anfinsen (1916–95)

CHRIS Anfinsen died suddenly on 14 May at the age of 79. He was the quintessential protein chemist, acutely aware of both the chemical and biological sides of the field. In 1972, while he was chief of the laboratory of chemical biology at the National Institutes of Health, he shared the Nobel prize in chemistry with Stanford Moore and William Stein, awarded for pioneering work relating the structure and function of the enzyme ribonuclease. At the time of his death he was professor of biophysical chemistry at Johns Hopkins University in Baltimore.

In the late 1940s, before even the structure of DNA was known, Anfinsen began an experimental study of protein biosynthesis. The incredible complexity of this process was then only just becoming evident, but the general outline and basic requirements were eventually laid out in his seminal book *The Molecular Basis of Evolution* in 1959. His careful thinking in this uncharted area was to serve him well.

The appearance in the mid-1950s of a large sample of the bovine enzyme pancreatic ribonuclease, provided with some foresight by the Armour Company, enabled him to diversify his activities in a more chemical direction. Although he worked on aspects of the amino-acid sequence of the ribonuclease chain, the sequence itself was largely solved by Stein and Moore at the Rockefeller Institute: it was only the second complete sequence to be determined. Chris and his team focused on the effects on the enzyme's structure and catalytic properties of covalently modifying the peptide chain by proteolytic cleavage and by chemical means. The possibility for modifying a specific sequence genetically was of course still decades away.

One modification he was trying to achieve was to reduce the four disulphide bonds in the native molecule to eight sulphydryl groups. No method could be found by which this reaction could be carried to completion without the use of a denaturing solvent such as 8 M urea to open up the molecule and



make the S–S groups accessible to the reducing agent. This process resulted in the complete loss of the enzyme's catalytic activity, but it was not clear whether this was due to the denaturing conditions, which was to be expected, or whether the conversion of the four S–S groups to eight SH groups might itself be enough to remove the activity.

To prepare a linear chain for sequencing, Stein and Moore also needed to cleave the disulphide groups, and chose oxidation to yield eight sulphonic acid functions; this reaction is irreversible, so all catalytic activity was lost. To no-one's surprise, the product in aqueous solution showed no evidence of any residual structure apart from a random coil.

In contrast to sulphonic acid groups, sulphydryl groups can readily be reoxidized to the disulphide form. Anfinsen dialysed away the urea from his reduced sample in an oxygen-free atmosphere: nothing seemed to happen. The solution was then left in a beaker open to the air. Overnight, a large amount of the original catalytic activity of the enzyme was restored — the protein had reformed its native structure, unaided! The enormous implications of this seemingly simple experiment were immediately obvious to Anfinsen: all the information necessary to convert the randomly coiled peptide chain into its unique, biologically active structure was contained in the sequence of amino-acid residues in the chain. Herein lay the answer to the last step in protein biosynthesis — straight chemistry, no biological 'magic'.

Confirmed in later years by dozens of papers from his own laboratory and thousands from others, this statement is the central dogma of what is now termed the 'protein-folding problem'. A detailed understanding of this eludes us even now, but the central fact still stands. The fascinating recent work on chaperonins has generated a whole new level of complexity, but the information transfer from gene to native structure remains dependent only on the sequence. A much longer review would be required to cover all of Chris Anfinsen's contributions to the chemistry and biology of proteins, but he will retain his major place in the history of science because of a simple experiment involving a beaker and a prepared mind. Frederic M. Richards

Frederic M. Richards is at Yale University, 260 Whitney Avenue, New Haven, Connecticut 06520, USA.