diffusion of spins when he studied the problem of disorder in quantum mechanics in his famous 1958 paper referred to above. The same framework of thought produced impressive contributions to the theory of superconductivity which had been opened up around that time by the BCS theory.

When Anderson took a joint appointment in Cambridge and at Bell Telephones, one of the great fruits of his time in Cambridge was his interaction with Sir Brian Pippard and with Brian Josephson, when Josephson was developing new ideas on superconducting tunnelling which led to his Nobel prize. The other big interaction in Cambridge was with Mott and many other British physicists which has produced many new ideas both in Cambridge and elsewhere in Britain, notably with Professor Thouless in Birmingham.

Anderson also did basic work on helium 3 over this period, and even the application of solid state ideas to astrophysics, but it is his work on the electronic structure of disordered systems and on magnetism which has earned him the Nobel prize. Other notable work on glasses has been on the low temperature thermal properties, and on disordered magnets, the 'spin glasses' where it has been my privilege to collaborate with him.

I have noted Anderson's early and continued interest in magnetism and how it has influenced his other interests. That interest was kindled by J. H. Van Vleck, who brought magnetism into the realm of quantum mechanics. It is astonishing to realise the rate of progress in understanding in the late 1920s and early 1930s when, compared to today, a small number of scientists revolutionised physics. Van Vleck published the first edition of his *Theory of Electric and Magnetic Susceptibilities* in 1932 and with this virtually the whole of the modern theory of magnetism was set up: not just solved because there are still deep and difficult problems remaining, but just how the classical theory could be absorbed into quantum theory, what the interactions had to be, how the Schrödinger equation was to be studied when crystal fields are present—it is all there, written out in a completeness and clarity which quite belie the date.

Subsequently Van Vleck developed and clarified many aspects of the electromagnetic nature of crystals, whilst also making major contributions to microwave and resonance spectroscopy, fields which have taken on new importance with the discovery of cosmic hydroxyl maser effects, and microwave communications. His work also extended to clarification of the nature of the chemical bond unifying the different valence bond and orbital pictures, but most importantly to the unification of the different models of magnetism. His Nobel award is something which his many advisers have been expecting for some years and gives just recognition for his achievement.  □

The Nobel prizes (2): Chemistry

# Thermodynamicist

## J. S. Rowlinson on Ilya Prigogine

THE Swedish Academy of Sciences has awarded this year's Nobel prize for chemistry to Professor Ilya Prigogine of the Université Libre of Brussels. He was born in Moscow sixty years ago but went to Belgium at an early age, and has spent his whole career there, although for the past ten years he has also held an appointment at the Center for Statistical Mechanics and Thermodynamics at the University of Texas.

Brussels has had a long tradition of research in classical or equilibrium thermodynamics, and although Prigogine has contributed to this field he has done his most important work in two other branches, statistical thermodynamics, which is based on molecular descriptions, and non-equilibrium thermodynamics. He started in the first with some war-time papers which developed the cell theories of liquid structure put forward in the 1930s by Lennard-Jones, and developed them to cover liquid mixtures also. Such theories suppose that a molecule spends most of its time in one of a lattice of cells to which it is confined by its neighbours. To be applicable to liquid mixtures such theories require that each species can be accommodated equally well in each cell.

This work, and parallel work in England and America in the 1950s, was a real advance, but was restricted in its useful application to mixtures of molecules of the same size. His book *Molecular Theory of Solutions* (1957) was influential in its day but is not much used now. The theory of liquids has developed along other lines which eschew the restrictive concepts of lattices or cells.

Meanwhile Prigogine was putting more of his effort into non-equilibrium thermodynamics, a subject which has had a long but not always very productive history. It started in the last century with the study of apparently simple transport processes such as the flow of electric current caused by a temperature difference between two junctions of different metals (Seebeck effect), or the inverse, the evolu-

tion of heat produced by an electric current across a metallic junction (Peltier effect).

Similar coupled flows of matter and energy occur when two fluids mix by diffusion, or when chemical reactions occur in inhomogeneous systems. Kelvin put forward quasi-thermodynamic explanations of some of these phenomena but it was not until 1931 that Onsager brought order to the whole subject by describing exactly how such forces and flows are coupled—his famous 'reciprocal relations' for which he was awarded the Nobel Prize for Chemistry in 1968. An interesting consequence of Onsager's work was Prigogine's discovery in 1945 that such systems are characterised by minima in the rates of entropy production.

These results are, however, limited to systems which are very close to equilibrium so that the flows are always proportional to the gradients of potential which generate them, such as temperature, or electric or chemical potential. They are, therefore, restricted in their applications, particularly if the systems are chemically reactive. One critic of this stage of development of the subject, believing that the useful results were not commensurate with the effort expended, said in 1966 that we should "ask not what we can do for irreversible thermodynamics; ask what irreversible thermodynamics can do for us". It was from this impasse t h a t Prigogine sought to escape.

Within the regime of linear laws he undertook the development of molecular or statistical theories of non-equilibrium thermodynamics. Until the 1950s such theories had been confined to dilute gases and had reached their climax with the work of S. Chapman and D. Enskog during the First World War. The methods they used, however, and even the name of the subject—the kinetic theory of gases—had little in common with equilibrium

*Prigogine*

statistical thermodynamics. Prigogine, Résibois, and others of the Brussels school have played a leading part in developing kinetic theories that are applicable to all fluids. One of the principal tools of this research has been to exploit the analogies between the Liouville equation, which describes how a molecular system evolves, and the time-dependent Schrödinger equation of quantum mechanics.

A second line of attack has been to push the macroscopic treatment of Onsager beyond the narrow range of situations in which flows depend linearly on forces. If this could be done then a whole range of new phenomena would come within the scope of non-equilibrium thermodynamics, such as the turbulent flow and convective instabilities of hydrodynamics, and chemically reactive systems that oscillate in space or time. However a macroscopic description implies that we can define such statistical properties as pressure, temperature and entropy even if the system is far from equilibrium. Prigogine showed that such an assumption is a sufficient condition for the use of thermodynamic methods and justified it in certain cases, for example, by showing that even in fast gas reactions the molecular distribution of velocities shows little departure from a local Maxwellian distribution.

The behaviour of fluctuations of these local properties distinguishes stable from unstable systems. Spontaneous fluctuations are always occurring but, except at a critical point, are usually unimportant. In a system with weak potential gradients each fluctuation quickly regresses to the steady-state behaviour, but when gradients are large then the fluctuations can grow until a new pattern of flow is established, for example the Bénard cells of rotating elements of fluid in a liquid heated strongly from below. Prigogine has sought to marry the classical theories of stability of structures with a generalised thermodynamics which would encompass such dissipative systems. He does this by introducing a 'local potential', which is a generalisation of the more familiar chemical potential, and then by using a variational principle to calculate the flows. The boundary between the stable or steady states and the dissipative structures is described by an 'excess entropy production' which is positive for the former and negative for the latter.

These new methods encompass many of the traditional ones used in discussing hydrodynamic instabilities, but their more interesting applications lie in the field of chemical reactions. This is, first, because reaction rates are, in practice, never linear in differences of chemical potential, and secondly because of the biological occurrence of systems in which complex chemical reactions are coupled to flows of matter and energy. He and his colleague, G. Nicolis, have used these methods to investigate the conditions under which reaction systems can oscillate in space and time with the aim of developing a thermodynamics that is applicable to biochemical systems.

Whatever new results emerge it is clear that Prigogine, both by his writings and by his enthusiastic advocacy, has changed the ways in which we can discuss a variety of difficult problems. He is, above all, a man or original ideas. In his book (with P. Glansdorff) *Thermodynamic Theory of Structure, Stability and Fluctuations* (1971), he quotes Bergson's saying of 1907 that the second law of thermodynamics is the most metaphysical of all laws of nature. He adds, "Whether a compliment or a criticism, this applies also to the 'generalised thermodynamics' we develop in this monograph".

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The Nobel prizes (3): Physiology and Medicine

# Starting a revolution

## Jesse Roth and J. E. Rall on Rosalyn Yalow

D R Rosalyn Yalow was awarded a Nobel prize for medicine and physiology in 1977 for the development of the radioimmunoassay. The introduction of the radioimmunoassay for plasma insulin in humans (R. S. Yalow and S. A. Berson, *Nature* **184**, 1648; 1959; *J. Clin. Invest.* **39**, 1157; 1960) started a revolution in endocrinology which spread from insulin to other peptide hormones including substances previously thought not to be antigenic, to steroid and thyroid hormones and to the cyclic nucleotides. Like other great revolutions it spread rapidly to encompass other fields including clinical pharmacology, enzymology, oncology, virology, immunology and haematology. The recent explosion of studies of cellular receptors for hormones, neurotransmitters, lipoproteins and drugs has its technical and intellectual roots in the radioimmunoassay.

Missing from the Nobel citation is the name of Dr Solomon A. Berson who died in 1972. Nobel prizes are not awarded posthumously, but historians and scientists everywhere recall the hundreds of joint publications of Yalow and Berson in the two decades that flank the publication of the seminal papers that introduced the radioimmunoassay.

To appreciate the revolution that the radioimmunoassay wrought it is necessary to recall the incredible state of endocrinology in 1960. The peptide hormones, which constitute about 80% of all hormones, could not, with rare exception, be measured in blood or other biological fluids. If one wished to study the dynamics of insulin *in vivo*, one could only guess from measurements of the blood glucose, or some other very distant component in the complex of reactions that regulate the blood glucose. Biological assays were available to measure the high concentrations of hormones in extracts of glands but these assays were orders of magnitude too insensitive and lacked the necessary specificity for measurements of hormones in blood.

How was it possible to measure peptide hormones at concentrations of $10^{-10}$ M in a sea of contaminating proteins at $10^{-3}$ M, when these hormones were virtually indistinguishable from thousands of other peptides and proteins in the blood? To solve this problem Berson and Yalow used antibodies to insulin, which they had recently characterised and had shown were capable of binding insulin but no other substances. Insulin that they labelled with radioactive iodine was reacted with antibody that had the desired specificity and the then unheard of affinity constant $10^{10}$ L/M. Conditions were set so that minute concentrations of unlabelled insulin competed with the labelled insulin for binding to the antibody. By measuring the ratio of radioactively-labelled insulin that was bound to antibodies to that which was free, the precise concentration of unlabelled insulin in the system could be determined.

This simple method of measurement of hormones in the blood was made possible by a series of conceptual leaps and technical innovations by Yalow and Berson in the preceding five years. They discovered that all insulin-treated patients generated antibodies to the hormone and recognised the problem of species specificity among insulins. They recognised the need to find antibodies with affinities so high as to be undreamed of by immunochemists of those days. They introduced methods to protect and purify proteins that were being labelled at high specific radioactivity. They devised a rapid precise method for separating antibody-bound hormone from free hormone and characterised in detail the kinetics and thermodynamics of insulin antibody interaction.