the sequences differ it is possible to deduce an idealised 'consensus sequence' using the most commonly found arrangements of bases. By analogy, translocation-specific DNA sequences may exist within the *T. brucei* variant antigen gene repertoire, one such sequence being associated with each gene. The degree of homology with the ideal 'consensus sequence' could then determine the frequency with which translocation occurred at that particular variant. Clearly sequences from genomic DNA clones will be of immense value in any further studies on the mechanism by which this protozoan Generator of Diversity operates. □

More sensitive immunoassays

from Roger Ekins

A NEW immunological assay method, claimed to be considerably more sensitive than radioimmunoassay, has recently been reported. C. Harris and coworkers have developed an 'ultrasensitive enzymatic immunoassay' (USERIA) applied in this instance to detect cholera toxin and rotavirus (*Proc. natn. Acad. Sci. U.S.A.* **76**, 5336; 1979). Radioimmunoassay (RIA) and related methods have played a vital part in endocrinology, and subsequently in other areas of biomedical science since their original development some 20 years ago. Fundamental to these techniques was their exploitation both of the structural specificity characterising antibodies and other specific binding proteins and of the sensitivity of 'signal detection' implicit in the use of radioisotopic labels. These attributes, in combination, provided the basis of assay methods of sufficient sensitivity and specificity to identify and measure the often minute concentrations of many biologically active substances present in biological fluids.

These techniques introduced a new principle into microanalytical methodology: that is, the estimation of the amount or concentration of a substance of interest (the 'analyte') by observation of its distribution between 'reacted' and 'unreacted' moieties following its interaction with a strictly limited amount of the specific reagent (antibody, for example) used. This principle differs from that underlying most traditional analytical methods in biochemistry, in which the estimate of the concentration of an analyte relies on observation of the effect on (or distribution of) a theoretically unlimited amount of a specific reagent following its interaction with the substance of interest for example, the measurement of a substance by exposure to light and observation of the extent of light conversion to fluorescent radiation. This principle underlies the immunoradiometric (IRMA) — 'radiolabelled antibody' — assay techniques developed a few years later in which excess of the specific reagent (radiolabelled antibody) is allowed to react with the analyte.

IRMA methods — like conventional RIA techniques — rely on a combination of the specificity of molecular recognition characteristic of antibodies (and other specific binding proteins) with the sensitivity inherent in radioisotopic measurement techniques. Nevertheless, although both IRMA and RIA methodologies possess many technical features in common, the contrasting analytical principles which they represent imply that they differ fundamentally both in their sensitivity and specificity characteristics, and in the overall incubation times required to carry out an individual measurement (Ekins in *Radioimmunoassay and Related Procedures in Medicine* **1**, 281, IAEA, Vienna, 1978). These distinctions arise largely as a result of the differing influence of the Law of Mass Action on the physicochemical reactions between analyte and specific reagent which constitute the basis of both analytical approaches. In particular, the 'labelled reagent' methods (such as IRMA) offer potential sensitivities many orders of magnitude higher than equivalent 'labelled analyte' assay techniques (such as RIA), primarily because the sensitivity of methods using the latter approach is essentially limited by the avidity of the specific reagent which reacts with the analyte, as revealed by the equilibrium constant of the reaction. This theoretical contraint does not apply to the sensitivity of 'labelled reagent' methods whose ultimate sensitivity limits are primarily imposed by classical considerations of signal-to-noise ratio, and implicitly by the 'specific activity' (observable events/unit time/unit mass) of the label used.

It is particularly in the context of 'labelled reagent' methodologies that labels other than radioisotopes are likely to offer significantly greater sensitivity and precision, together with absence of bias and shorter assay times. They may also circumvent the problems and hazards of handling radioisotopes which have frequently, though not always legitimately, been advanced as a reason for the ultimate abandonment of the current generation of radioassay methods.

Enzyme-linked immunosorbent assay (ELISA) methods — conceptually identical to IRMA techniques and differing only in their substitution of an enzyme for a radioisotopic label — provide an example of a non-isotopic labelled reagent method which has proved valuable, for example, in agriculture (for the identification of plant viruses) in tropical medicine, and in other biomedical contexts, particularly those in which sophisticated instrumentation is out of place. Nevertheless, conventional ELISA methods have generally — though not invariably — failed to attain the high sensitivities which are implicit in the labelled reagent approach, essentially because the 'noise' (consequent upon 'non-specific' labelled antibody binding) is sufficiently large in relation to the 'signal' (generated by the specifically-bound antibody/enzyme-label complex) to preclude the detection of very low levels of individual analytes.

So the recent description, by Harris and coworkers (*Proc. natn. Acad. Sci. U.S.A. op. cit.*) of their ultrasensitive enzymatic radioimmunoassay is of considerable interest. Aside from the further terminological confusion inflicted on an already chaotic area of nomenclature, their methodological refinement is notable insofar as it utilises a radioactive substrate (^{3}H-AMP) for the quantitation of the specifically-

Roger Ekins is Professor in the Department of Nuclear Medicine, The Middlesex Hospital Medical School, London.

100 years ago

Artificial Diamonds

An unusually large audience gathered at the Royal Society last Thursday to hear Mr. Hannay's account of his artificial diamonds.

The President, after inviting discussion of the paper by Messrs Hannay and Hogarth, observed that probably the large audience had assembled more especially in consequence of the general interest attaching to the next paper on the artificial formation of the diamond, and he felt that the valuable investigation just detailed showed Mr Hannay to be a person worthy of attention when he claimed to have made even so startling a discovery as that on the face of this next communication. With regard to this the President observed that the attitude of science was always sceptical, and the Society would need ample proof that the metamorphosis of carbon into diamond had been really effected. . .

The President having called for any observations on the notice by Mr Hannay, Mr Maskelyne said that the present differed from the numerous announcements and other communications that have been heretofore made to scientific societies at various times purporting to record the artificial production of the diamond in this, that here the product so claimed to have been manufactured is really diamond. He had himself proved this by the simple tests of the mineralogist. He had deeply abraded topaz and sapphire with a particle of the substance and abraded them with the greatest ease; the angle of the cleavages of a crystalline fragment sent him by Mr Hannay was the angle between faces of the regular octahedron, and he had burnt a small grain of the substance on a platinum foil with the characteristic glow of the diamond, and without its leaving a residue.

From *Nature* **21**, 4 March, 421; 1880.

0028-0836/80/10014-02$01.00