measured synchronously, and their small changes subjected to covariant analyses (Scheffé, 1953) using a computer. The logical steps involved in defining causal relationships are described. The results are expressed not as reproducible, or reversible, relationships between variables, but as reproducible probabilities of finding such relationships.

The method has potential value in the study of drug effects on intact natural systems.

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The multiple emulsion formulation for the slow release of drugs.

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Multiple emulsions are water-in-oil emulsions which are redispersed in a second aqueous phase. Such emulsions have the advantage of being much less viscous than the primary water-in-oil emulsion and can be easily injected through a fine bore needle. The use of such emulsions as an alternative to the Freund type antigen-carrying adjuvant (water-in-oil emulsion) was suggested by Herbert (1965). Such a formulation for the slow release of drugs has been developed in our department since 1965.

The release of drugs from multiple emulsions is dependent on at least two types of mechanism, the break-up of larger particles and the osmotic gradient between the internal and the continuous aqueous phases. It can be influenced by altering three parameters, the osmotic gradient between the two aqueous phases, the internal phase volume and the concentration of the detergent necessary to form the primary water-in-oil emulsion. The release rate can be assessed by *in vitro* and *in vivo* methods.

The preparation of multiple emulsions will be demonstrated, as well as their naked eye and microscopic appearance. Examples of slow release of drugs from such emulsions will be shown using an *in vitro* technique as well as results of biological assay. The effect of manipulating the three parameters on release rate will be illustrated.

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A method of investigating ureteral activity in the rat.

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Although the existence of a nerve supply to the ureter has been demonstrated (Wharton, 1932; Gruber, 1933; Lapides, 1948) the nature and function of this nerve supply is still in doubt. In an electron microscopic examination of the upper ureter of

the rat Notley (1968) observed both afferent and efferent fibres and an apparent absence of ganglia, perhaps indicating that the ureter is innervated only by sympathetic fibres.

Methods of investigation have included *in vivo* and *in vitro* techniques where results have been obtained by direct observation, recording intraluminal pressure, measurement of isotonic muscle contraction, ureteral electromyography and forms of ureteral radiography. Each method, however, suffers from disadvantages which could seriously influence the results obtained or severely limit the scope of investigation.

The method demonstrated here allows measurement of the peristaltic rate and the flow of a perfusing solution along the ureter. Peristaltic rate is measured by recording the action potential of each peristaltic wave using a flexible-tipped glass microelectrode inserted into the outer muscle coat. This has the advantage that mechanical stimulation and damage to the ureter is minimal.

The microelectrodes are pulled mechanically from soda glass tubing (1·0 mm external diameter, 0·75 mm internal diameter) to have a shank length of 15–20 mm and a tip diameter of approximately 4 μm. These dimensions have been found to give the tip the flexibility which is required for the measurement of action potentials from a tissue as mobile as the ureter. The electrodes are filled under vacuum with 3 M KCl and those having a resistance of less than 10 MΩ are accepted for use. The microelectrode is linked to the pre-amplifier via an agar-KCl bridge and Ag/AgCl electrode.

By tying off both the renal artery and renal vein urine production is prevented and perfusion of the ureter is carried out through a fine needle inserted into the pelvis of the kidney. The flow of the perfusion fluid is measured photoelectrically, while the incorporation of 0·002% w/v Evans's blue in the perfusion solution facilitates visual observation.

This method allows investigation of the effects of renal pelvic pressure, autonomic drugs and, with some modification, autonomic nerve stimulation on the rat ureter.

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A method for studying release of prostaglandins from superfused strips of isolated spleen.

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In response to nerve stimulation or adrenaline, dog spleens contract and release prostaglandins (E_2 and $F_{2\alpha}$) into the venous effluent; these effects are blocked by phenoxybenzamine (Ferreira & Vane, 1967; Davies, Horton & Withrington, 1968; Gilmore, Vane & Wyllie, 1968). This effect has now been investigated by a simple *in vitro* method.

Prostaglandin release from superfused strips of rabbit spleen was detected by isolated tissues suspended in cascade below the spleen (Fig. 1). Selectivity of these assay tissues was enhanced by infusing a mixture of antagonists at point B. On infusion of a