DEMONSTRATIONS

An isolated programmable stimulator for the determination of ventricular fibrillation threshold

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The determination of the electrically-induced ventricular fibrillation threshold in open-chest anaesthetized dogs is a useful test for potential anti-fibrillatory drug activity. Vulnerability to ventricular fibrillation may be determined by passing trains of constant current pulses through bipolar epicardial electrodes during the T wave of the ECG, and increasing the current intensity until fibrillation ensues. The heart is then defibrillated by DC shock and the determination repeated at intervals. Drugs that reduce the asynchrony in recovery of excitability of myocardial fibres raise the fibrillation threshold; myocardial ischaemia, which increases the inhomogeneity of recovery processes, reduces the threshold (Moore & Spear, 1975).

The stimulator described here is designed to operate automatically. It enables repeated determinations of the threshold to be performed with maximum reproducibility, and avoids the tedious attention required using a manually-operated system. The stimulator delivers trains of constant current rectangular pulses at intervals to the fibrillating electrodes, either during pacing or with the heart in spontaneous rhythm. Pulse train delay following ventricular activation (QRS) and train duration are both variable, and atrial pacing is interrupted automatically for 1 s after stimulation. The current intensity of successive pulse trains is increased automatically by a preselected value (0.1–9.9 mA) until fibrillation occurs. Further delivery of pulse trains is then stopped automatically by operation of a blood pressure level detecting circuit in the stimulator, and a warning sound is emitted so that defibrillation can be performed without delay.

The R wave is detected in the stimulator and initiates a variable delay before generating a pulse train (Figure 1). During pacing, part of the pacing signal is used to prevent accidental triggering by the pacing

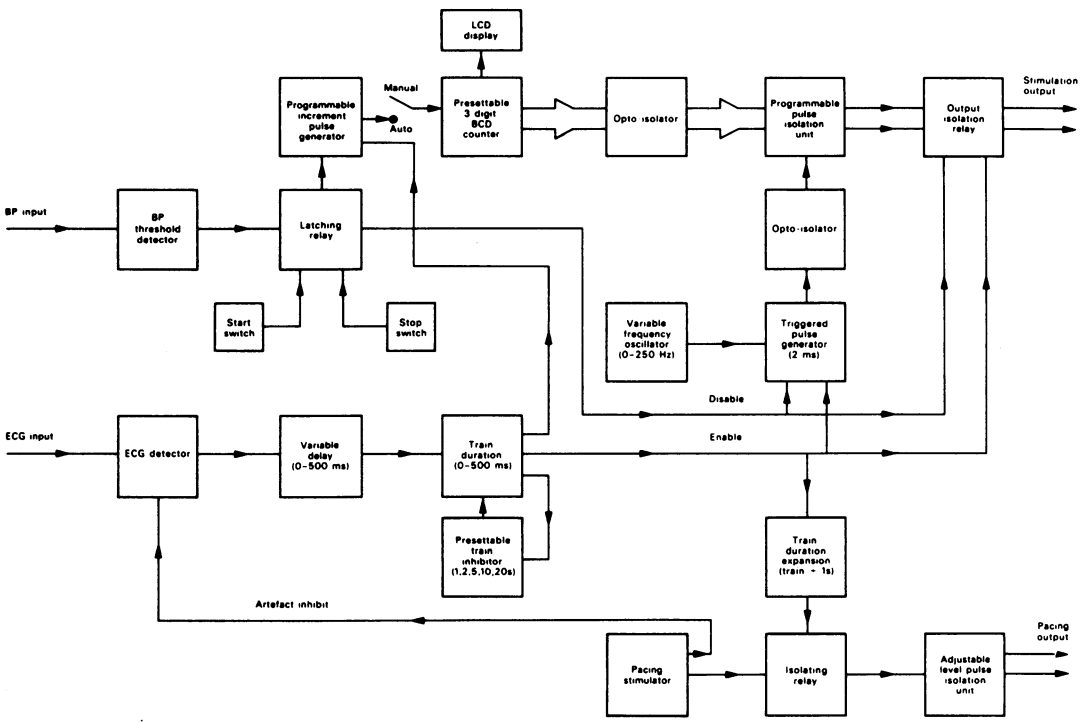

Figure 1 Arrangement of the programmable stimulator for determination of ventricular fibrillation threshold.

artefact in the ECG waveform. The pulse train consists of 2 ms pulses at an adjustable repetition rate determined by a variable frequency oscillator, and these drive the pulse isolation unit. The current output is determined by the contents of the binary-coded decimal (BCD) counter. The initial value of the output current is pre-set by thumbwheel switches. Successive pulse trains are delivered after a pre-selected minimum interval, and incremented automatically by a pre-selected amount.

Reference

MOORE, E.N. & SPEAR, J.F. (1975). Ventricular fibrillation threshold. Its physiological and pharmacological importance. *Arch. int. Med.* **135**, 446–453.

The use of K-sensitive electrodes to study drug-induced release of K from suspensions of isolated hepatocytes

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Many cells respond to hormones and neurotransmitters with an increase in membrane permeability which, if maintained, may result in substantial net movements of ions. These movements can be studied by means of ion-sensitive electrodes which may be intracellular or extracellular. The aim of the demonstration is to illustrate how an extracellular K-sensitive electrode can be used to give a rapid and continuous record of the K movements that follow the application of a range of agonists to guinea-pig isolated hepatocytes. This preparation was chosen because liver cells can be obtained in large quantities and they possess a number of different receptors each of which can increase K permeability, though not necessarily by the same mechanism (for a review see Putney, 1978). The resulting net losses of cell K can be readily recorded as increases in extracellular K concentration by means of a K-sensitive electrode placed in the cell suspension. The method is equally applicable to the study of net K movements in tissue slices prepared e.g. from the liver or salivary glands (Batzri, Selinger, Schramm & Robinovitch, 1973).

The electrodes are based on the use of the K-selective ionophore valinomycin which is incorporated in a PVC membrane in the way described by Band, Kratochvil & Treasure (1977). A minor modification of their procedure was to form the membrane on a support consisting of a disc of filter paper (dia. 2–4 mm) placed in the end of a piece of PVC tubing. Electrodes made in this way are more selective than commercially available K-sensitive glass electrodes, and are also much less expensive.

References

BAND, D.M., KRATOCHVIL, J. & TREASURE, T. (1977). An ion selective electrode for the determination of potassium. *J. Physiol.*, **265**, 5P.

BATZRI, S., SELINGER, Z., SCHRAMM, M. & ROBINOVITCH, M.R. (1973). Potassium release mediated by the epinephrine α-receptor in rat parotid slices. *J. biol. Chem.*, **248**, 361–368.

PUTNEY, J.W. (1978). Stimulus-permeability coupling: role of calcium in the receptor regulation of membrane permeability. *Pharmac. Rev.*, **30**, 209–245.

Currents recorded from single acetylcholine-activated ion channels in skeletal muscle membrane

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A demonstration will be given of the technique, due to Neher, Sakmann & Steinbach (1978), for recording current flow in small areas of membrane, electrically isolated by means of a polished glass pipette pressed against the cell surface. Recordings will be shown of current flow due to the opening of single ion channels, activated by acetylcholine or suberyldicholine, and the changes produced in these currents by the action of local anaesthetic drugs.

References

NEHER, E., SAKMANN, B. & STEINBACH, J.H. (1978) The extracellular patch clamp: a method for resolving currents through individual open channels in biological membranes. *Pflugers Arch.*, 375, 219–228.

Pharmacological analysis of leptazol induced epileptogenic activity in the anaesthetized rat

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Studies on folic acid induced epileptogenic kindling in the rat

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GABA and benzodiazepine modification of ^{14}C glutamate release from rat spinal cord slices

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Voltage clamp recording from rat submandibular ganglion cells

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