1 Introduction

A substantial number of papers have already been published on the subject of intracellular measuring systems and related amplifiers. Among them are very sophisticated designs for simultaneous measurement and stimulation of the preparation under study using voltage and current clamp techniques (Wilson and Goldener, 1975; Koppenhöfer and Schramm, 1974). Substantial effort has been put into guarding of inputs and proper shielding (Suzuki et al., 1978). It is necessary to neutralise input capacitance to improve the frequency response of the measuring system (Wood, 1981; Sachs and Specht, 1981). In a number of applications this neutralisation may become difficult where the input circuit presents large capacitances. Compensation will result in a substantial increase of noise and one has to compromise between speed of response and excess noise.

It is clear that stray capacitances can be reduced by situating the input circuit close to the preparation, which is common practice. However, this introduces a major problem in a configuration where large power levels are applied to the preparation, as in our case.

One of the studies in our laboratory is concerned with the response of membrane potential and force of contraction to stepwise changes in temperature. For this purpose high-frequency (HF) alternating currents are applied to the preparation under study at power levels up to 50 W at a frequency of 30 MHz. Owing to large HF components induced in the input circuit and earthing loops between the measuring probe and peripheral equipment, saturation of a common amplifier resulting from nonlinear behaviour of the amplifier chain makes accurate measurements impossible.

To guarantee reliable results, it was necessary to completely reconsider the design of a microelectrode amplifier as commonly used in such an experimental setup.

2 Design considerations

Interference from the HF power source is coupled into the amplifier chain along two paths. One way is direct coupling of the HF signal through the microelectrode tip, which measures the transmembrane potential, into the input circuit of the amplifier. This interference can be attenuated by application of an HF field that is symmetrical with the respect to the preparation and so also with respect to the position of the microelectrode tip. This is achieved by a centre tap on the transformer which couples the HF power into a small chamber in which the preparation is situated. The centre tap is connected to a reference electrode in the plane of symmetry of the chamber (Goovaerts and Metselaar, 1985). Proper positioning of the microelectrode reduces the HF component produced at the input of the amplifier to a minimum. Additional filtering in the input circuit removes a major part of the remaining HF signal.
The second way along which HF interference is introduced in the signal path is formed through earthing loops between the reference electrode and peripheral equipment. These loops act as antennas at the frequency of the HF heating power and produce an interference signal source in series with the desired signal from the microelectrode amplifier. Attenuation of this interference is possible by isolation of the microelectrode amplifier from the surrounding equipment.

The principle of isolation, applied to standard instrumentation configurations for electrophysiological measurement, has been described earlier (Van Heuningen et al., 1984). It will be shown below that application of the method to the measuring system under consideration provides a substantial improvement in interference suppression.

The input configuration of the system to measure transmembrane potentials is essentially different from that which measures other bioelectric signals. For most bioelectric measurements a differential input circuit is common. The circuit attenuates interference of signals which are effective on both electrodes in equal phase: this is called common-mode rejection. No such effect is present in the asymmetrical arrangement which is usually applied in microelectrode amplifiers.

The left hand side of Fig. 1 shows the simplified diagram of a microelectrode amplifier configuration with the main components influencing the bandwidth of such a system. The right hand side of the picture shows a substitution diagram for a correctly compensated amplifier.

It can easily be seen that, if shielding is properly carried out and the total stray capacitance of the shielded part is kept small, i.e. $C_2 \gg C_1$, the interfering source $E$ will produce a major interference signal across $C_1$. In most cases it is possible to guard the reference electrode by connecting the shield and the reference electrode (jumper at 'a') to withdraw practically any interference signal active on both the input and the reference electrode in the asymmetrical configuration.

Hence, it can be concluded that an asymmetrical layout of the input circuit will perform as well as a differential circuit in rejecting interference signals when isolation is applied between the measuring input and amplifier output.

The required compensation of input capacitance, which is mainly produced by the attached microelectrode tip, raises an additional problem. Compensation is commonly achieved by a 'feedforward' of variable gain which, in the isolated configuration, has to be controlled from outside the isolated part. Furthermore, another signal path is required for adjustment of the compensation, measurement of electrode impedance and stimulation purposes.

Several solutions can be presented regarding the isolation of compensation loop, signal or calibration generator and amplifier. In fact only two solutions are relevant, and these are shown in Figs. 2 and 3.

### 2.1 Solution 1

Isolation of the input buffer circuit only as shown in Fig. 2 also requires isolation of the return signal for capacitance compensation and, if required, isolation of the stimulating current.

The advantage of this configuration is that the input circuit draws very little current, which can easily be supplied by the isolation amplifier's isolated power output. A major disadvantage of this approach is the construction of the compensation loop. The compensation signal passes two isolation ports and acquires a time delay. The bandwidth of isolation amplifiers is commonly limited to a value below 100kHz and so the effect of compensation is substantially degraded.

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**Fig. 1.** Simplified diagram of a microelectrode input stage with the main bandwidth-limiting components under isolated conditions. The right hand side shows the substitutional diagram of such a configuration, showing the increased influence of shielding on the effectiveness of an interference source $E$ in an isolated configuration. $R_m$ and $C_m$ represent the membrane, $R_e$ is the microelectrode resistance and $C_p$ is the total input capacitance without compensation, compensated for by $-C_i$. $R_i$ represents the input resistance of the amplifier.

**Fig. 2** Block diagram for an isolated input buffer. The compensation loop passes two isolation ports, introducing a substantial reduction in compensation loop bandwidth.

**Fig. 3** Isolation of the input amplifier and compensation circuit resulting in wideband operation and greater stability compared with the situation in Fig. 2.