AN ENGINEERING DESIGN STUDY FOR METHODS OF DETECTING OVULATION

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Introduction

Considerable effort is currently directed towards obtaining a complete physical and endocrinological understanding of ovulation. Significant changes in hormone levels may take place within hours of the time of ovulation. It is essential to be able to correlate these changes with the physical process of ovulation to give a definitive datum point.

The first attempts to directly detect ovulation in a reasonably precise manner were reported by Burr in 1935 (1). Since that time, despite continued efforts, no satisfactory solution has been found. This paper examines the reasons for this failure and discusses the significant issues that must be resolved. Some of the engineering difficulties encountered in this work by our group, over the past two years, are described.

Programme

Our work has been primarily directed towards:

1. Increasing the understanding of local phenomena around the ovary associated with ovulation.
2. Critically evaluating and comparing various methods of transducing ovulation into signals enabling remote detection.
3. Developing a method for visually observing ovulation to evaluate proposed transducer design.
4. Designing a telemetry system to implement long-term experiments.

The way in which this work fits into the overall research programme is shown in Fig. 1. From this it will be apparent that work is current at several points of the diagram. This is necessary since each aspect involves much refinement before it can be considered satisfactory.

Study of Local Changes Associated with Ovulation

The release of the mature ovum from the surface of the ovary is associated with the development and rupture of a small cyst-like swelling on the surface. This swelling, the follicle, contains a quantity of fluid together with the group of cells surrounding the ovum itself. The rupture is controlled by its size and the presence of (unknown)substances in the blood. In animals with no regular estrous cycle, such as the rabbit as used in our work, rupture may be induced by the injection of Chorionic Gonadotropin (2). This injection causes ovulation some 9 to 13 hours later.

There have been reports of several lines of current research into the detection of ovulation. Long-term monitoring of ovarian temperature has been investigated for some years (3), and the measurement of potentials around the ovary has been noted (4), though not thus far reported as viable. Since no solution adequate for our needs was found in the literature, we proceeded to draw up a list of alternative approaches.

In an order roughly corresponding to what appears to be the present possibility of success, some of the alternatives are:

- measurement of potential on ovary surface
- local impedance changes
- local temperature changes - taking the difference between the two ovaries to accenuate such changes
- detecting the release of follicular fluid with radoactive tracers
- monitoring the size of the ovary, or the change in acoustic properties with ultrasound
- detecting the pressure change within the ovary associated with the release of follicular pressure on rupture

The basic mechanism of ovulation is similar across a broad range of species, which allows a wide choice of animals for experimental work. The ease of producing ovulation in the rabbit, together with suitable cost and size, make it convenient for exploratory studies of the above possibilities. The ovary in the rabbit is about 1 cm long, large enough for testing transducers with reasonable hope of comparison to the situation in larger animals. Surface potential changes during ovulation have been measured. Using a micro-pipette electrode, the potentials across the membrane of the follicle may be found (5). This has shown that the follicular fluid is normally some 10-15 mV negative with respect to the surface. Of interest is the possibility of change in the surface potential when the follicular fluid is released. To monitor such changes the ovary is exposed, and surrounded with oil to prevent heat loss by evaporation from the surface. Electrodes placed on the surface have on occasion detected abrupt changes in potential at ovulation, but there have been many instances of ovulation without measurable surface change. Investigation of this anomaly continues. It has been difficult to repeatedly achieve ovulation, a further frustration. It this can be overcome then rabbits will continue to used to evaluate the other possibilities for detection, as mentioned above

Observation of Ovulation over Long Periods of Time

Despite the similarity of reproductive physiology with humans, the rabbit will not completely serve the purposes of the overall project since it is not capable of supplying sufficient blood for the quantity of hormone assays intended. To effect this the experiments are extended to sheep, and this requires verification of any proposed system for detecting ovulation by correlating the signals from the system with the visual observation of ovulation. To enable this a Teflon window has been made to give direct observation of the ovary. A sheep with such a window is shown in Fig. 2

In using the window in about 12 animals over a 16 month period, follicle development and regression has been seen 3 or 4 times. Development of improved methods - such as a fibre optic culdoscope

- continues in order to increase the reliability.

Telemetry

Work with sheep, and the projected work in monkeys and humans, requires monitoring of ovarian parameters over periods of weeks. To allow mobility of the subject, radio telemetry is required.

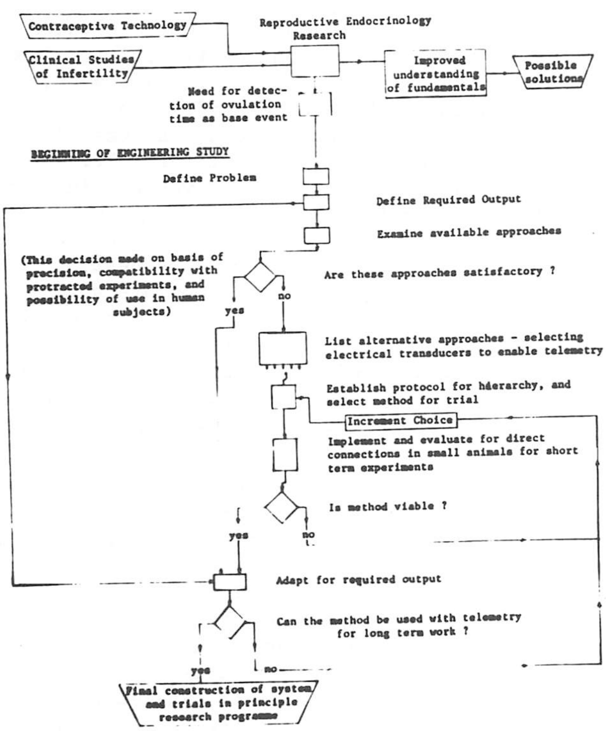

Figure 1. Outline for engineering study of methods of detecting ovulation.

There is a considerable volume of literature covering many aspects of telemetry. Work was started to develop a system capable of monitoring the d.c. voltages from electrodes, and a design that has been evaluated in the last year in use on sheep is outlined in Fig. 3. This will monitor low d.c. voltage over periods of months. The circuit has an input impedance of 5 MΩ; a maximum sensitivity of below 1 mV; and a drift over a week of below 10 mV with the electrodes connected to ovarian tissue.

Improvements which are proposed for this design include using micro-power integrated circuits as the input amplifier to further reduce the drift, and incorporating orthogonal antenna array at the receiver to mitigate possible loss of signal in some positions of the transmitter.

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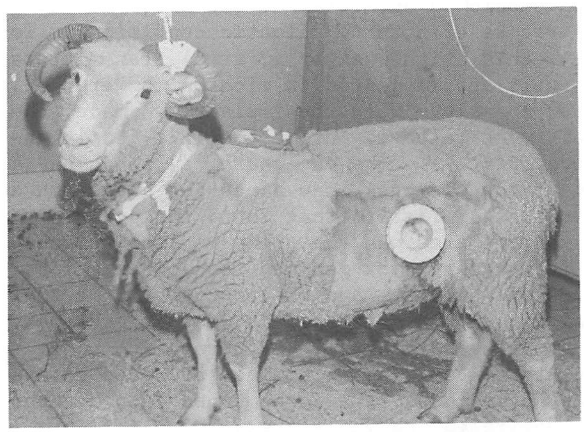

Figure 2. Dorset sheep used in long-term visualisation. Teflon window in flank contains ovary. Prototype transmitter is strapped to back, and venous catheter taped on horn.

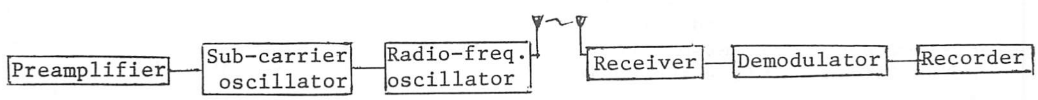

Figure 3. Outline of telemetry system used for potential measurement