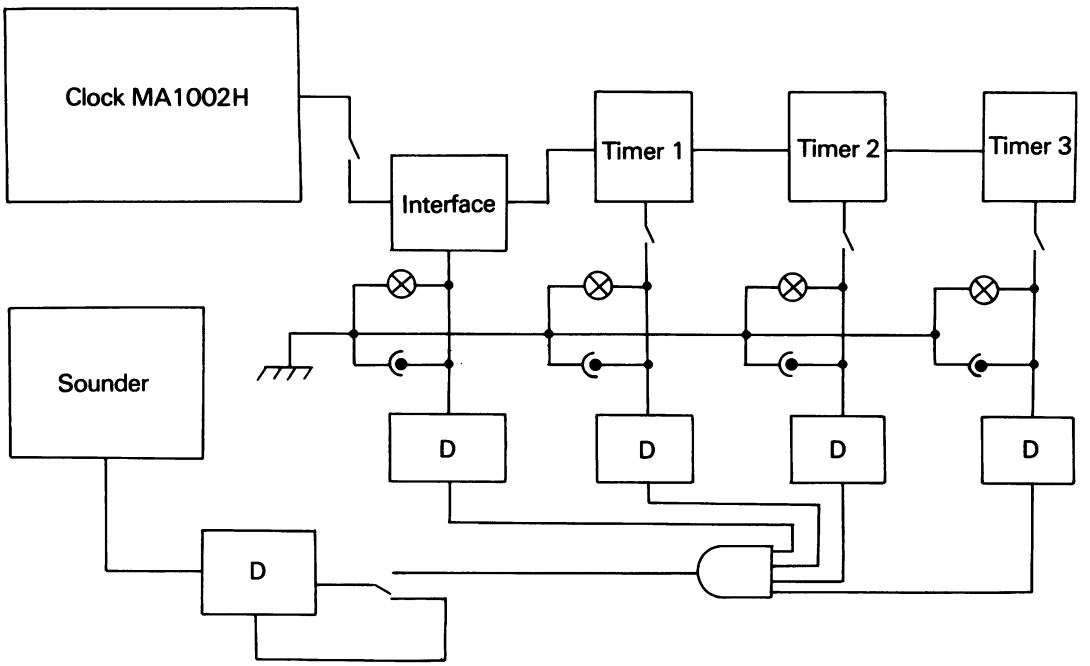

Figure 1 Schematic diagram of the alarm/timer. D is a disenabling gate for the alarm circuit.

Production of prostaglandins by porcine endothelial cells in culture

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Cultured endothelial cells were prepared from porcine aorta by 30 min digestion with 0.2% collagenase (De Bono, 1974). Cells were incubated at 37°C in 24–72, 1 ml, chambers containing Waymouth medium, 17.5 mM HEPES buffer, and 17.5% inactivated foetal calf serum. The medium was changed at 3 days. At 6–8 days, when the cells were confluent monolayers (2 cm^2, 8×10^4 cells/chamber), the supernatants were pooled, extracted with diethyl ether at pH 3–4 and assayed for prostaglandins (PGs). The supernatants were replaced with serum-free Eagles MEM medium with 17.5 mM HEPES buffer to which test substances were added, and the chambers returned to the incubator for one hour. These supernatants were extracted and assayed individually.

Pooled 3–5 day supernatants from nine different cell culture batches were assayed by bioassay and radioimmunoassay (RIA) using antisera to PGE_2 (cross reactions: $PGE_1 = 30\%$, $PGF_2\alpha = 1.4\%$, 6-oxo-$PGF_1\alpha = 0.03\%$) and $PGF_2\alpha$ (cross reactions: $PGF_1\alpha = 17.5\%$, $PGE_2 = 0.02\%$). Prostaglandin production varied between cell culture batches. Results were: PGE_2 (RIA) $= 68 \pm 19$ ng/ml, $n = 9$, range $= 27–189$; PGE_2 (rat stomach strip) $= 74 \pm 28$ ng/ml, $n = 6$, range $= 32–210$; $PGF_2\alpha$ (RIA) $= 38 \pm 7$ ng/ml, $n = 3$, range $= 27–52$.

Prostaglandins of the 'E' and 'F' types were separated by thin layer chromatography in ethyl acetate:formic acid (80:1). The immunoreactive materials co-chromatographed with authentic standards. The prostaglandins were further characterized by arachidonate-induced human platelet

aggregation in order to distinguish between PGE_1 and PGE_2, and to investigate the possible presence of 6-oxo-$PGF_1\alpha$, the stable end-product of prostacyclin (PGX) which would be expected to be produced by these cultured cells (Moncada, Gryglewski, Bunting & Vane, 1976). The 'PGE' fraction did not inhibit platelet aggregation, showing that PGE_1 was not present in significant amounts. Some inhibitory activity was detected in the 'PGF' fraction indicating that 6-oxo-$PGF_1\alpha$ might be present.

Bradykinin (1 μg/ml) increased PGE production during 1 h from a basal level of 5.2 ± 0.7 ng/ml to 13.7 ± 4.0 ng/ml (measured as PGE_2 by RIA, means of four separate cell culture batches). This is a similar phenomenon to that observed with human endothelial cells stimulated with angiotensin II (Gimbrone & Alexander, 1975). Lower doses of bradykinin (1 ng/ml) also significantly increased PGE from 3.9 ± 0.3 ng/ml to 6.6 ± 0.5 ng/ml ($P < 0.01$, Students t-test) (1 experiment, $n = 5$ replicate cultures). Indomethacin (1 μg/ml) reduced PGE production by $33 \pm 5\%$ when given with bradykinin (1 μg/ml) and, in another experiment, by $83 \pm 1\%$ when given as an additional 30 min pretreatment ($n = 5$ replicate cultures in each experiment).

The production of the vasodilators, PGE_2, and possibly prostacyclin, by endothelial cells in culture, may be analogous to situations *in vivo* where the endothelium is regenerating, e.g. in graft vascularization where we have been measuring elevated blood flow by ^{133}Xe clearance (Lewis, Peck, Williams & Young, 1976).

The increase in prostaglandin production in cultured endothelial cells induced by vasoactive substances such as bradykinin, may be related to prostaglandin production in inflammatory responses *in vivo*, and to prostaglandins detected in perfusates from tissues *in vitro*. (Results: mean ± s.e. mean)

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The cardiovascular and uterine effects of labetolol in conscious normotensive pregnant rats

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Labetolol, an antagonist at both α- and β-adrenoceptors (Farmer, Kennedy, Levy & Marshall, 1972) has been shown to be an effective hypotensive agent in hypertensive dogs and rats (Brittain & Levy, 1976) suggesting a clinical use in hypertension. This work investigates the effects of labetolol in the conscious, normotensive pregnant rat on blood pressure and uterine activity.

Pregnant rats (Sprague-Dawley) were prepared with an intrauterine microballoon and jugular cannula on Day 19 of gestation (Day 1 = Day of mating) as described previously (Whalley & Riley, 1977). A polyethylene cannula (PP50 tubing) was also placed in the carotid artery for recording blood pressure. The three tubes were exteriorized through a stainless steel template sewn subcutaneously in the back of the neck. Uterine activity and blood pressure were recorded by Bell and Howell pressure transducers and displayed on a Grass polygraph recorder. Uterine activity was quantified by means of a polygraph integrator (model 7P10B). Cardiovascular effects were recorded on Day 20 and uterine activity recorded continuously from Day 20 up to parturition.

The maximum fall in blood pressure after giving labetolol as a bolus dose intravenously on day 20 of gestation was 18.0 ± 5.1 mmHg ($n = 6$) after 1 mg/kg and 26.4 ± 3.4 mmHg ($n = 6$) after 10 mg/kg. No effect on uterine activity was observed on Days 20, 21 or 22 of gestation (given daily from day 20) with 1 mg/kg labetol ($n = 6$). Small transient increases in uterine activity were observed on each day after labetolol (10 mg/kg).