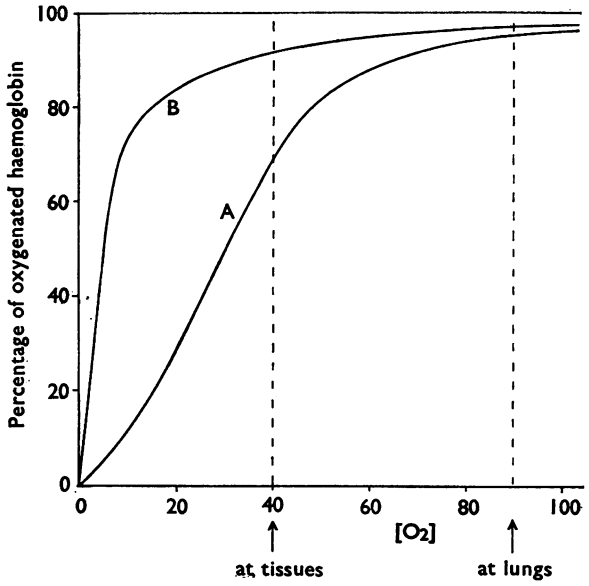

FIG. 1. Abscissa, partial pressure of oxygen in mm Hg. Ordinate, percentage of protein in the oxy form. Haemoglobin dissociation in the presence of 2,3-diphosphoglycerate is described by the sigmoid A (Benesch & Benesch, 1970), and shows cooperation between the subunits. Curve B is a rectangular hyperbola theoretically predicted by Michaelis–Menton kinetics.

The shape of curve A is due to the fact that the conformation of the four protein subunits in haemoglobin changes slightly on taking up and releasing oxygen (Perutz, 1968). The position of the curve is also regulated by the naturally occurring small molecule 2,3-diphosphoglycerate (DPG) which can bind to a specific site on the haemoglobin when it is in the deoxy conformation, and hence tends to stabilize that conformation (Benesch & Benesch, 1970). The DPG binding site consists of amino and imidazole groups arranged to complement the shape and charge of the DPG molecule when the protein is in the deoxy form (Arnone, 1972). However, in oxyhaemoglobin the shape of the site changes so that it can no longer admit DPG.

The combination of DPG with haemoglobin may be analogous to a drug-receptor interaction, and models have been built to study this interaction at the molecular level. The large model can be positioned in either the oxy or deoxy conformation, but this quaternary change is accompanied by alterations of tertiary structure within the protein, which cannot be shown. Two smaller non-working models have therefore been built to display the DPG interaction site more accurately in its oxy and deoxy forms.

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Some persistent effects of the pre- and neonatal administration of psychotropic drugs on noradrenaline metabolism in discrete areas of rat brain

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Werboff & Gottlieb (1963) have described behavioural abnormalities in the offspring of rats treated with psychotropic drugs during pregnancy. In view of the probable asso-

ciation between brain monoamines and behaviour, it was of interest to see if the administration of drugs during the pre- and neonatal periods might produce permanent alterations in catecholamine metabolism in the central nervous system. Preliminary experiments (Tonge, 1972) have shown that chlorpromazine, methylamphetamine and phencyclidine administered during the pre- and neonatal periods have persistent effects on whole brain monoamine concentrations. Since the turnover rates of monoamines in different areas of the brain may be of more relevance than absolute concentrations, the depletion of noradrenaline after synthesis blockade with 300 mg/kg of α-methyl-*p*-tyrosine has been examined in eight areas of rat brain.

TABLE 1. *Percentage depletion of noradrenaline (4 h after α-methyl-p-tyrosine) from the brains of rats exposed to psychotropic drugs during the pre- and neonatal periods*

	Controls	MA	CPZ	MA+CPZ	PH	IM
Cortex	46	59	38	40	67	49
Hippocampus	42	62	13	23	41	44
Striatum	54	43	29	50	25	36
Thalamus	41	45	55	55	53	45
Hypothalamus	41	60	5	26	35	38
Amygdaloid	42	26	19	29	48	39
Mid-brain	30	44	10	28	29	30
Pons/medulla	59	53	52	58	59	51

Controls=ascorbic acid only; MA=methylamphetamine; CPZ=chlorpromazine; MA+CPZ=methylamphetamine+chlorpromazine; PH=phencyclidine; IM=imipramine.

Methylamphetamine (80 mg/l.), chlorpromazine (200 mg/l.), phencyclidine (200 mg/l.) and imipramine (200 mg/l.) have been administered in the drinking water of rats during pregnancy and suckling. All drug solutions included ascorbic acid and one group of rats received ascorbic acid solution only. The offspring received no further drugs after weaning, and the rates of depletion of noradrenaline after synthesis blockade were determined nine months later in eight areas of the brains of male rats. Methylamphetamine, chlorpromazine and phencyclidine all affected both the concentrations of noradrenaline and the depletion rates after synthesis blockade; imipramine was without effect. These results suggest that noradrenaline metabolism may be permanently altered by exposure to psychotropic drugs during the pre- and neonatal periods.

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A simple low-cost circuit for the programmed application of ejecting and retaining currents in microelectrophoresis experiments

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Microelectrophoresis experiments usually consist of the alternate application of ejecting and retaining currents to the various drug solutions contained in a multi-barrelled micropipette. It is usual to apply ejecting current pulses of standard intensity and duration; however, theoretical considerations (Bradshaw, Roberts & Szabadi, 1973a) and experimental observations (Bradshaw, Roberts & Szabadi, 1973b) now indicate that it is essential to keep the intensity and time of application of the retaining current constant throughout the experiment.

We have developed a low-cost timing circuit which enables the programmed application of ejecting and retaining currents to up to four electrophoresis channels in a regular cycle. The circuit consists of four timer 'units' (I–IV) operating in sequence; each unit consists of an 'ejection timer' (E) and a 'retention timer' (R). The timers are driven by a 12V DC supply, and operate reed switches which control the application of electrophoretic currents. More than one channel may be operated simultaneously by each