signals used for IMP calculations were obtained from 4 placements of the sensitive surface in each serial measurement.

A set of serial recordings obtained by a sensor placed in the myocardium is shown in Figure 2. Each output signal shows a different amplitude and characteristic contour specific for the position of the sensor. The $V_{\parallel}$ deep increases sharply to point A for about 0.08 sec (isovolumetric systole phase) prior to the rise of the aortic curve. Then the increment clearly slows down and comes to a termination at E, a point which coincides with the end of systole on the aortic curve (this period corresponds to ejection phase). In the recording of $V_{\parallel}$ middle, the initial rise to A is small, while the slow rise thereafter is still clear. $V_{\perp}$ middle shows a larger deflection than $V_{\parallel}$ middle and its configuration consists of a sharp rise, followed by a very slow rise which almost forms a plateau during the ejection phase. $V_{\perp}$ deep shows a negative deflection in clear contrast to the curves obtained at the other 3 placements; slightly prior to the aortic rise, the curve begins to fall downwards. IMP's were calculated as P_1 and P_2 of equations (1) and (2) using the peak amplitude of V's. Since the IMP's calculated by the equations represented pressure acting in a direction parallel or perpendicular to the base-apex line, these IMP's were also suffixed by $_{\parallel}$ or $_{\perp}$. The peak amplitudes of V's and calculated IMP's are summarized in the Table. $IMP_{\parallel}$ deep, i.e. longitudinal IMP in the deep portion, was slightly smaller than the systolic aortic pressure and largely exceeded $IMP_{\perp}$ deep, the circumferential IMP in the deep portion. The $IMP_{\perp}$ middle was larger than $IMP_{\parallel}$ middle but did not attain $IMP_{\parallel}$ deep. After measurements, the ventricle was isolated and boiled in a saturated salt solution containing a small amount of detergent for 2 h. The myocaridal fibre of the ventricles could then easily be skinned off, permitting a simple inspection of its direction. The fibre orientation was circumferential in the middle portion and almost parallel to the base-apex line in the deep portion. These observations indicated that the directional non-uniformity of IMP may have been due to the variation in myocardial orientation. These results seem to coincide qualitatively with the results obtained using a strain gauge arch, where different contractile forces were also observed at different positions[1,2]. The ventricle is not a simple thick-walled ellipsoid, but has a fine structure consisting of contractile fibres and densely distributed vascular network. Such a structure may produce the conditions where the summation of the contractile forces becomes a vectoral IMP.

Pulsatile deflections of output signal (V's) and calculated longitudinal and circumferential intramyocardial pressure (IMP's) in the middle and deep portions of the left ventricular myocardium

	Volts			mm Hg		p[a]
	Mean	SD		Mean	SD	
$V_{\parallel}$deep	0.237	0.029	$IMP_{\parallel}$deep	121.0	16.6	
$V_{\parallel}$middle	0.069	0.018	$IMP_{\parallel}$middle	72.6	10.2	<0.01
$V_{\perp}$deep	−0.083	0.031	$IMP_{\perp}$deep	6.4	2.3	<0.01
$V_{\perp}$middle	0.137	0.024	$IMP_{\perp}$middle	97.8	13.9	<0.05

Mean and SD of 7 serial measurements. Abdominal aortic blood pressure was 130/100 mm Hg on the average. [a] Student's t-test, indicating the statistical difference of values as compared to $IMP_{\parallel}$-deep.

[1] E. H. Sonnenblick and E. S. Kirk, Cardiology *56*, 302 (1971/72).
[2] N. W. Robie and W. H. Newman, J. appl. Physiol. *36*, 20 (1974).

A Heated Stage and Tissue Culture Chamber for Electrophysiology

L. Bonkowski and H. I. Runion[1]

University of the Pacific School of Pharmacy, 751 Brookside Road, Stockton (California 95211, USA), 15 April 1976.

Summary. A simple, inexpensive heating circuit is described for use with a warmed microscope stage, small tissue bath, and heated tissue culture chamber. A major consideration in the design of the apparatus is a compatability with electrophysiological studies. Thus, proper shielding and low profile for microelectrode positioning are featured.

This paper describes a heating system which is suitable for use in electrophysiological studies of avian and mammalian tissues in vitro. A warmed microscope stage with tissue bath and a warmed tissue culture chamber are presented. In each device, continuous, controlable heat is provided to a vibration-free, perfusable chamber. There is adequate access to the tissue for microelectrodes, and when grounded, the aluminium warming portions of each device act as an effective Faraday shield to the preparation, reducing the necessity for a separate cage.

Heating circuit. The design of the heating system is simple (Figure 1). A feedback controlled operational amplifier and power transistor form the basis of the proportional heating, temperature control system. Thermistors in a bridge configuration provide the necessary input information to the operational amplifier. One thermistor serves as an ambient temperature sensor (AIR) to detect and create compensation for heat dissapation changes that result from variations in room temperature. The second thermistor (BATH) is encapsulated within the aluminium of the warm stage or culture chamber near the heating element and monitors chamber temperature.

When the device is cold, the high resistance of the BATH thermistor will unbalance the bridge to increase the potential difference across the inputs of the operational amplifier. The transistor (NPN 2N3055) controls the power in the heating circuit. An increased voltage applied to the base will increase the current supplied to the heating element. As the device warms, the resistance of the BATH thermistor will decrease, lowering the potential

[1] Acknowledgment. We wish to thank William F. Dryden for his helpful comments and advice in apparatus design.

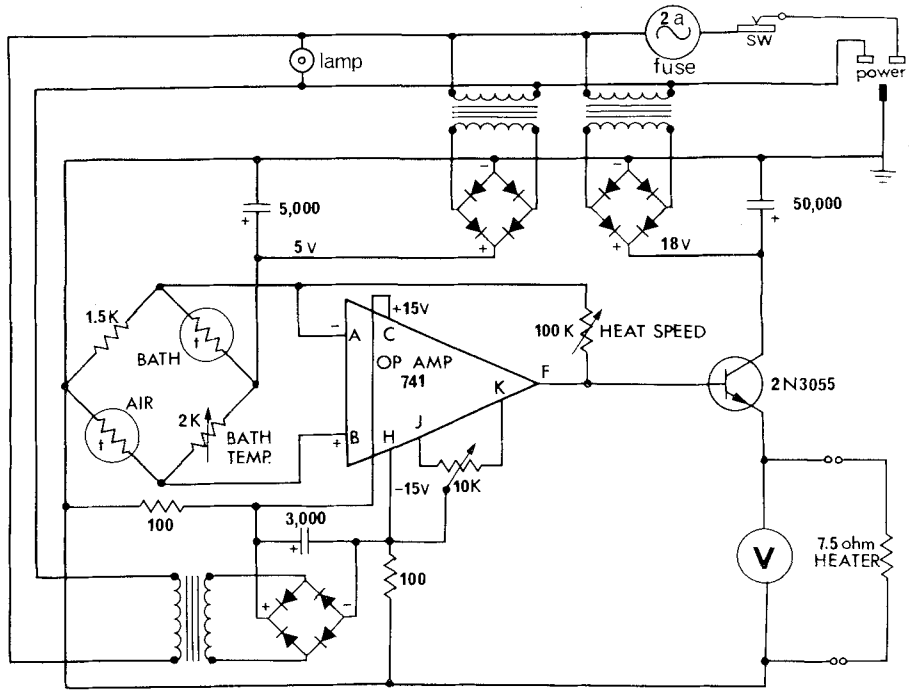
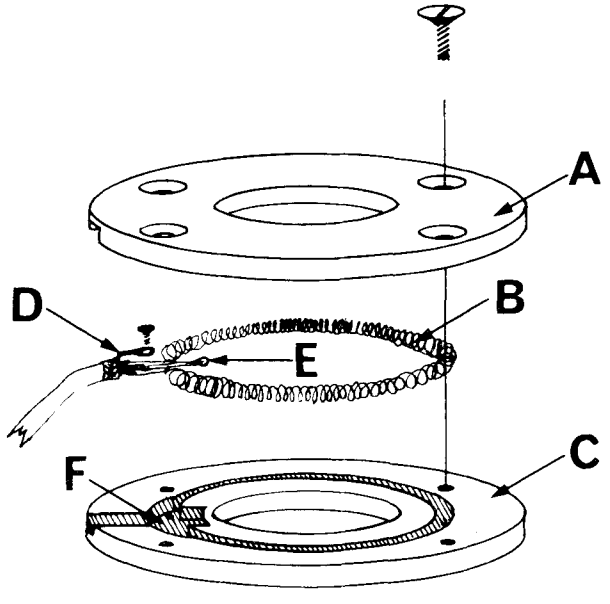
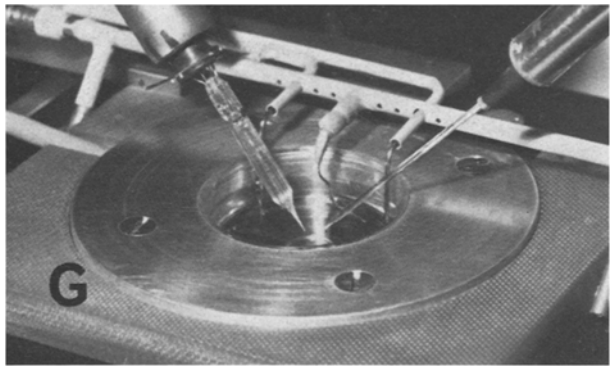


Fig. 1. Circuit Diagram. Resistance values are in ohms. Capacitance values in microfarads. BATH and AIR thermistors are identical bead type, typical resistance 2K at 20 °C (Radio Spares Cat. No. TH-B12 151–029[2]). Overated power requirements for the 3 power supplies are: ± 15 V, 500 mA; 5 V, 500 mA; 18 V, 3 Amps. The 2K BATH TEMP. potentiometer is a ten-turn miniature or trim potentiometer. The 7.5 ohm heater running at about 10 volts will maintain a 250 *g* warming collar at 37 °C in a 20 °C room. Larger devices or greater temperature differences may require more power in the heating circuit.





difference across the operational amplifier and decreasing the voltage to the base of the transistor. Warming will progressively slow until final equilibrium temperature is reached. The 2K ohm BATH TEMP. potentiometer adjusts the degree of imbalance necessary in the thermistor bridge to create the required supply of current through the heating element once the desired equilibrium is achieved. The HEAT SPEED potentiometer controls the amount of feedback within the circuitry of the operational amplifier, and ultimately determines the temperature fluctuations that will occur in the warming device by limiting or augmenting the influence that a resistance change in an arm of the bridge has on the output of the amplifier. Thus, a high resistance in the feedback loop will bring about a rapid warming of the apparatus, but result in greater fluctuations in chamber temperature. A low resistance value will cause slower warming of the apparatus but result in a finer temperature control once equilibrium is reached. In practice, it is best to leave the apparatus switched ON permanently, and set the HEAT SPEED resistance at about 1K ohms. Under these conditions, the temperature within the bath may be maintained within 0.03 °C and remain unchanged at perfusion rates (prewarmed perfusate) of up to 1 ml per min in a 5 ml bath.

[2] Radio Spares Components Ltd., P. O. Box 427, 13–17 Epworth Street, London EC2P 2 HA, England.

[3] L. BONKOWSKI and W. F. DRYDEN, Brain Res., in press (1976).

←

Fig. 2. Warm Stage. A, C) Top and bottom of stage machined of aluminium. B) Coiled nichrome wire heating element (sleeved in heat-shrinkable insulating tubing before final placement). D) Grounded shield of supply cable which screws to shell of stage. E) BATH thermistor. F) Groove machined into sections A and C to house heating element B and thermistor E. G) Photograph of warm stage in use in an electrophysiological study using cells in culture[3].

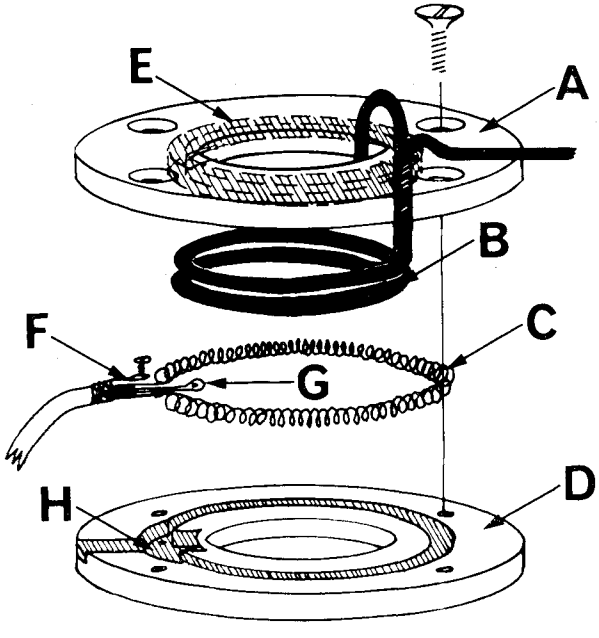
Direct current is used to power the heating element (coiled nichrome wire or low resistance element) for minimal 50/60 cycle interference. All wires are shielded, and the aluminium shell which houses the BATH thermistor and heating element is grounded to reduce electromagnetic interference.

Warmed stage and chamber. Figures 2–4 show various applications of the heating method in electrophysiological investigations on isolated preparations and cells in culture. Figure 2 illustrates the use and construction of a warm stage attached to a mechanical stage of an inverted microscope for a tissue culture study. The centre of the stage is machined to accomodate 30 mm plastic petri dishes, allowing routine cell culture procedures to be employed in the growing of the tissue. Removal of the top of the dish during experiments allows access to the bath for recording microelectrodes as well as the introduction of the reference electrode and perfusion lines which are incorporated into the gassing manifold positioned over the stage.

Figure 3 illustrates a warming collar used with a tissue bath suitable for studies on isolated preparations. The centre of the device is once again machined to fit 30 mm plastic petri dishes. In this way, the same warming collar may be used with a variety of specially modified dishes, each optionally constructed for a specific tissue or experiment. Since viewing is from above in this set up, the

[4] A. F. R. Wolfe, W. F. Dryden and I. G. Marshall, *The Synapse.* Proc. of the Scot. Electrophys. Soc. (Blackie & Son, Glasgow, March 1976).

[5] L. Bonkowski and H. I. Runion, Proc. West. pharmac. Soc. *16*, 221 (1973).



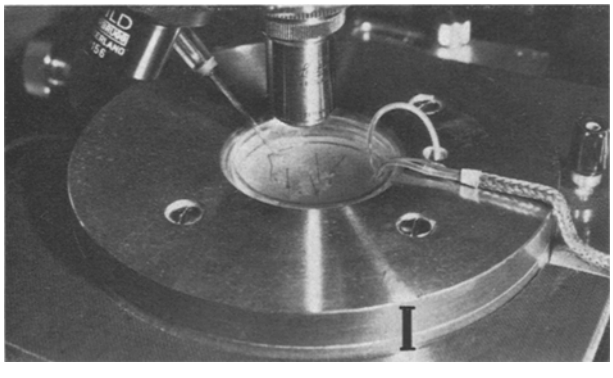
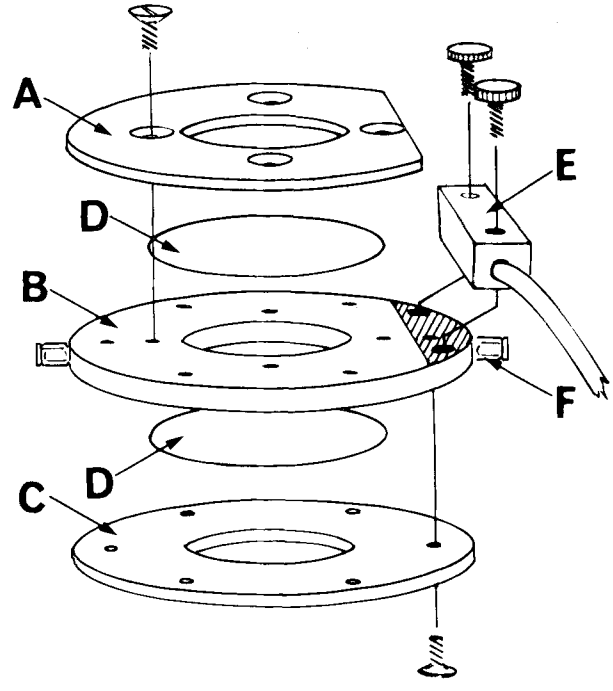


Fig. 3. Warming collar for small tissue bath. A) Top section of machined aluminium including groove E which houses coil of perfusion line B for prewarming of fluids entering the bath. C) Coiled nichrome wire heating element (sleeved in heat-shrinkable insulating tubing before final placement). D) Bottom section of machined aluminium including groove H which houses the heating element C and BATH thermistor G. F) Grounded shield of supply cable which screws to bottom section D. All spaces surrounding the components within the collar are filled with silicone grease for best heat transfer before the apparatus is finally bolted together. I) Photograph of waruing collar in use in an electrophysiological study on an isolated preparation[4]. Notice perfusion line entering the bath after prewarming (within groove E).



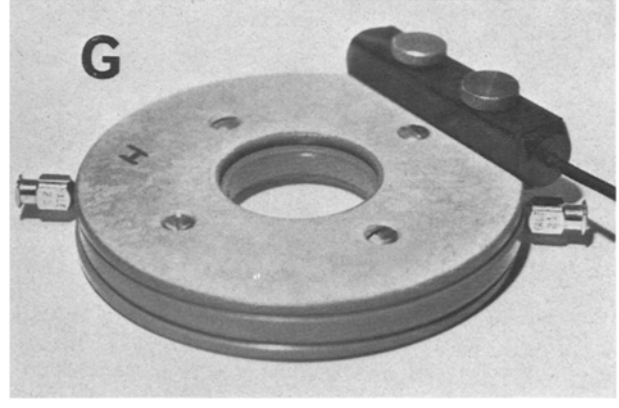


Fig. 4. Warmed tissue culture chamber. A) Top section of chamber. B) Centre section of chamber to which top and bottom attach. C) Bottom section of chamber. D) No. 1 glass cover slips. E) Warming block which contains the heating element and BATH thermistor. Attaches to centre section of chamber by 2 thumb screws. F) Hypodermic needles which serve as inoculation and perfusion ports. Most surfaces are teflon coated for minimum tissue reaction within the chamber and easy release of the glass cover slips. The area where the warming block attaches to the chamber is left uncoated for efficient heat transfer. G) Photograph of assembled culture chamber with warming block attached[5].

extremely low profile of the stage in Figure 2 is not necessary, and the inclusion of a groove in the aluminium shell of the collar to house a coil of perfusion tubing is possible. This allows preheating of perfused substances to the same temperature as the bath.

Figure 4 depicts the warmed tissue culture chamber. In this device, a warming block contains the heating element and thermistor, and transfers heat to the chamber when attached by 2 thumb screws. One warming block is used for a number of chambers, which are kept in a conventional incubator until needed on the microscope stage. The chambers may be sterilized, fully assembled, by autoclaving, and inoculated with cell suspension via the hypodermic needles which also serve as perfusion ports during electrophysiological experiments. The top and bottom of the chamber attach separately to the centre section to allow removal of the top cover for electrode placement without disturbing the other seals of the chamber. Thin glass cover slips form the top and bottom of the tissue bath, ensuring excellent optical clarity and permitting the use of extremely high power, short working distance objectives.

Aluminium was selected as the material best suited for the fabrication of the devices described. It is easily machined. It has a very high thermal conductivity which allows efficient, even distribution of heat, and good electrical conductivity for shielding. Before final construction of each device, heat-shrinkable insulating tubing is placed around the heating element and BATH thermistor to insulate them from the shell which is grounded through the shield of the supply cable. Any remaining space is filled with silicone grease to ensure maximum heat transfer.

CONGRESSUS

France

17th International Congress of Physiological Sciences

in Paris, 18–23 July 1977

The first two days will be devoted to general lectures and during the last four days specialized meetings will take place. Further information can be obtained from the National Physiological Society of each country or by writing to the Congress Secretary: Prof. J. Scheerer, Secrétariat du 17. Congrès Int. des Sciences Physiologiques, U. E. R. Pitié-Salpêtrière, Cedex 1300, F–75300 Paris-Brune, France.

The Netherlands

The 7th European Food Symposium on product and process selection in the food industry

at Eindhoven, 21–23 September 1977

The symposium will be organized by the Food Working Party of the European Federation of Chemical Engineering in cooperation with the Dutch Society of Nutrition Science and Food Technology and IUFoST. Topics: 1. Food industry and society; 2. Product and process selection: procedures and techniques; 3. Examples of product selection based on economic considerations; 4. Examples of process selection based on economic considerations. Further informations by the Food Working Party, c/o Gesellschaft Deutscher Chemiker, P.O. Box 90 04 40, D–6000 Frankfurt 90, Federal Republic of Germany.

PRAEMIA

Applications Invited for 1977–78 Johananoff International Fellowship for Advanced Biomedical Studies

The Johananoff Fellowship, awarded by the Mario Negri Institute Foundation Inc., New York, and the Mario Negri Institute for Pharmacological Research in Milan, Italy, amounting to $ 15,000 for one year, was established in 1974 through the farsightedness and generosity of Mr. S. Johananoff, a distinguished international industrialist. The Johananoff Fellow will spend a sabbatical year at the Mario Negri Institute in Milan, free from laboratory duties, administrative and other routine, thinking out an Advanced Study critically reviewing achievements in one of the following fields: cancer chemotherapy and/or -immunology, cardiovascular pharmacology, neuropsychopharmacology or drug metabolism.

Candidates for the Fellowship should be non-Italian, mid-career scientists, internationally known for their work on one of the above topics. Applications should include a curriculum vitae, list of publications and outline of proposed studies, and must be received in Milan by 31 January 1977. Requests for application kits should be airmailed to: The Johananoff Fellowship Committee, Ist. di Ricerche Farmacologiche Mario Negri, Via Eritrea 62, I–20157 Milano (Italia). Tel. (02) 355 4546. Telex 37268 NEGRINST.

Prix Friedrich Miescher

A l'occasion du centième anniversaire de la découverte des acides nucléiques, la Société Suisse de Biochimie a crée un prix Friedrich Miescher, octroyé par l'Institut Friedrich Miescher (Société Ciba-Geigy, Bâle). Les candidatures (Suisses ou Suisses à l'étranger) doivent être adressées au Secrétaire de la Société Suisse de Biochimie: C. Bron, Institut de Biochimie, chemin des Boveresses, CH–1066 Epalinges.