

The performance of the octopus circulatory system: A triumph of engineering over design

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Summary. Despite the very considerable difficulties presented by the basic molluscan anatomy and the possession of a blood pigment with an oxygen carrying capacity that never exceeds 4.5 vols%, the cephalopod circulatory system contrives to deliver oxygen at a rate fully comparable with that of an active fish. This is achieved by adding accessory pumps to push blood through the gills, by a multiplicity of pulsatile veins and by raising the systemic blood pressure considerably above the levels found in other molluscs. Detailed control of blood distribution is a necessity in a system where the peripheral resistances may be expected to change dramatically when the animal starts to move and large parts of the central nervous system are apparently dedicated to this task. In this account we have reviewed blood pressure and flow at rest and in exercise. We have further examined the evidence which indicates how the animals modulate the cardiac output, drawing attention to the very different response found in cephalopods and the higher vertebrates.

Key words. Octopus; circulatory physiology; exercise; hypoxia; cardiac control.

Introduction

The rate and manner in which blood must be pumped round a body depends on the principal functions of the blood. These can include the need to deliver the products of digestion, eliminate wastes and distribute chemical messengers. However, in a large and active animal, with an almost totally aerobic metabolism, it is above all the function of the system to deliver oxygen. This is the situation we find in the cephalopods and it is this requirement which is of overriding importance in our consideration of the cardiovascular system.

The Mollusca is almost certainly a monophyletic group, and the cephalopods have evolved from smaller, less active animals, with basic design features common to all molluscs, including a mantle cavity with gills that empty first into atria and then into a ventricle. In many molluscs the venous return, to the gills and heart, is channelled first through a series of blood sinuses, which also serve as the hydrostatic skeleton. In cephalopods this fluid skeleton is much reduced, replaced by muscles acting directly against muscles, antagonists arranged to squeeze each other out, often in a direction determined by complex tissue lattices^{25,55}. The circulatory system has ceased to have a locomotor function and is considerably restricted in volume. At the same time, its operating pressure has had to rise. If muscle extends muscle, by squeezing, the arterial blood pressure should be high enough to overcome the considerable peripheral resistance, generated when the animal starts to move, in addition to the inherent resistance derived from the small diameter exchange vessels which close the system¹⁰. The process of progressive elimination of extensive blood sinuses, allied to a steady increase in blood pressure, can be traced by comparing the situation in *Nautilus* with *Octopus* and squids³⁹.

The basic mollusc design, with the gills upstream of the systemic heart, means that the blood is likely to be at very low pressure by the time it reaches the gills, having passed through the body musculature and the peripheral vascular bed. That may not be particularly important for a bivalve or gastropod, where water flow across the gills is powered by cilia and relatively slow. In a cephalopod, with its high oxygen demand, water is forced through the

gills much more rapidly, pumped by the mantle musculature⁶⁶. The blood passes the gills quickly and must be brought into intimate contact with the ventilatory water flow, which in turn means a second set of capillaries in the gills. The pressure of the venous return must be boosted to overcome this second set of peripheral resistances. Cephalopods manage this in two ways. Many of the veins, and the lateral venae cavae in particular, are contractile. And all cephalopods, including *Nautilus*, have accessory branchial pumps^{6,7}. The dibranchiate cephalopods have gone further and developed branchial hearts at the base of the gills, further increasing the pressures generated by the great veins. Figure 1 summarises the general anatomical situation, and figure 2 gives details of the hearts and related structures in an octopus.

A third feature of the basic design, which helps to set a limit to what is possible in performance terms, is the strange situation with relation to blood pigments. Elsewhere in the molluscs, both haemoglobin and haemocyanin are found, and the former may even occur concentrated in blood corpuscles (haemocoelic erythrocytes in several species of bivalves; see Read³⁶). Cephalopods seem to be limited to haemocyanin, a very high molecular weight, copper-based, oxygen carrier, never found in blood cells. Restricted by viscosity, this carrier never builds up to concentrations capable of transporting more than about 4.5% of oxygen. Fish blood typically has a carrying capacity of over twice as much.

The routine performance of the circulatory system

1. Pressures and frequencies

The ventricle. Diastolic and systolic pressures, measured in the dorsal aorta of *Octopus vulgaris* a few centimeters downstream of the ventricle, vary considerably between individuals, or even within the same individual at different times⁵⁷. Resting values in the region of 2.0 kPa in diastole or 3.5 kPa in systole are typical of animals in the 400–1000 g range, at a temperature of 20–24°C. Heart-beat frequency at this size and temperature is around 0.75 Hz. At lower temperatures the magnitude of the pulse in the aorta, the mean diastolic pressure and the frequency, all decrease; values around 1.0–1.5 kPa and 0.4 Hz are

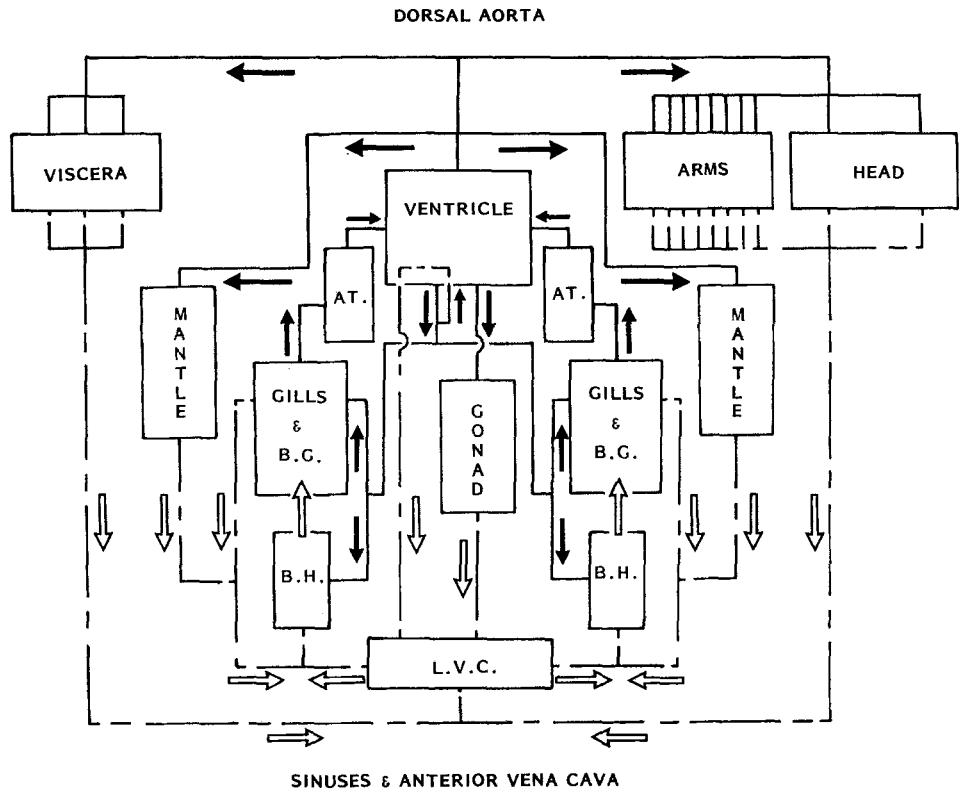


Figure 1. Schematic diagram of the major elements comprising the octopus cardiovascular system. Of the ventricular aortae, the dorsal feeds the greater part of the systemic vascular bed, with the gonadal running to

the gonads and the abdominal delivering oxygenated blood to the cardiac organs, gills and vessels (see fig. 2); AT, atrium; B.G., branchial gland; B.H., branchial heart; L.V.C., lateral venae cavae.

found at 15°C⁵⁷. Slightly higher values have been recorded from the much larger *Octopus dofleini* at 10°C (2.1–2.9 kPa in diastole, and 3.6–6.1 kPa in systole at rest)⁴¹. Pressures in the aortae do not directly reflect the intra-ventricular pressures. The properties of the aortic wall, particularly in the case of the dorsal aorta, will modify the pulse form. *The role of the dorsal aorta and arterial vessels.* All animals with powerful systemic hearts and significant peripheral resistances, face the problem of the pulsatile nature of cardiac output. Flow, to the systemic vasculature is energetically expensive if delivered in a undamped, pulsed manner. Smoothing out the flow is critical. Mammals achieve this by incorporating compliant reservoirs in the form of the large arteries, working in accordance with transmission line theory⁴¹. The cephalopod has also developed a compliant reservoir but in this case it can be modelled as a straightforward windkessel⁴¹. The presence of a cephalopod windkessel was first proposed by Johansen and Martin²³. It works by transferring

the kinetic energy imparted to the blood on ventricular contraction, to potential energy in the rubber-like molecules in the walls of the dorsal aorta³⁸, which is then transferred back to the blood during ventricular diastole. The characteristics of this system have now been described in some detail³⁹⁻⁴¹. Gosline and Shadwick¹⁵ have further shown that the stiffness characteristic of the aorta is species-dependent. Less active cephalopods, such as *Nautilus* have thin-walled, large-volume vessels, whereas squid, such as *Notodorus*, have thick-walled, low-volume vessels, more similar to those of vertebrates. Although *Nautilus* and *Octopus* have true windkessels, the squids may gain some relatively minor benefit from wave propagation effects¹⁵. It must also be realised that the arteries of cephalopods are muscular and have an extensive nerve supply^{4,17}. More than a million neurones in the brain appear to be dedicated to the innervation of the blood vessels⁷⁰. Excised lengths of aorta show almost continuous muscular activity when inflated to physiological pressures, and respond in a complex manner to putative neurotrans-

Table 1. Flow along the aorta in freemoving *Octopus vulgaris*. Values in ml · kg⁻¹ · min⁻¹ (frequency in Hz; stroke volume in ml · kg⁻¹) (extract from Wells et al.⁶¹)

Animal	Weight (g)	Recovery from anaesthetic (max)	At rest (min)	In exercise (max)	In recovery after exercise (max)
X3	2516	31 (0.90; 0.57)	25 (0.80; 0.53)	43 (0.78; 0.92)	35 (0.87; 0.79)
X12	2387	34 (0.86; 0.65)	28 (0.77; 0.60)	48 (0.85; 0.94)	44 (0.85; 0.86)
X26	1745	42 (0.73; 0.90)	32 (0.58; 0.91)	36 (0.57; 1.04)	48 (0.57; 1.40)
X44	1735	67 (0.83; 1.34)	50 (0.83; 0.99)	56 (0.80; 1.16)	57 (0.78; 1.01)
X51	1117	80 (0.75; 1.77)	47 (0.78; 1.00)	111 (0.95; 1.95)	89 (0.95; 1.57)
X47	1018	59 (0.87; 1.14)	38 (0.63; 1.01)	104 (0.98; 1.76)	78 (0.83; 1.57)

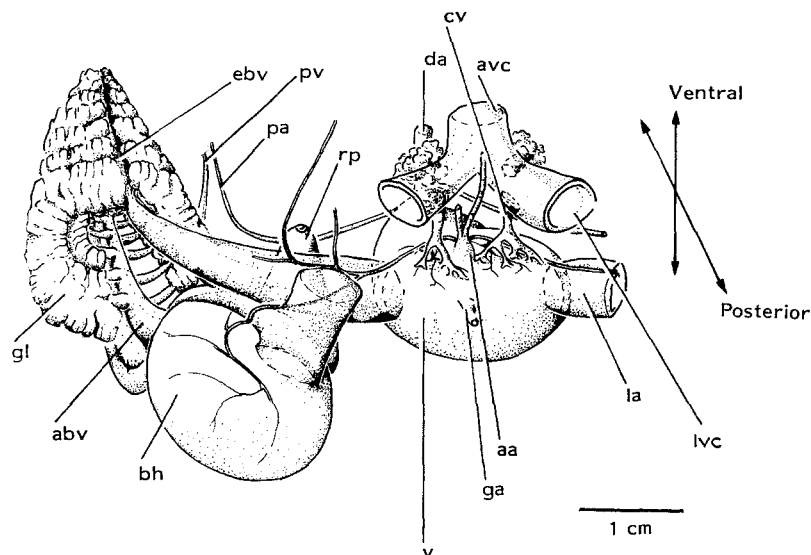


Figure 2. The main cardiac organs and vessels of the octopus, *Eledone cirrhosa* (after Smith⁴⁸). aa, abdominal aorta; abv, afferent branchial vessel; avc, anterior vena cava; bh, branchial heart; cv, coronary vein; da,

mitters, such as 5-hydroxytryptamine, and acetylcholine^{40, 62}. It would seem almost inevitable that the central nervous system controls the properties of the windkessel and the distribution of resistance in the smaller vessels. A clear role could be in the regulation of flow patterns during activity, as seen in other molluscs²⁶.

Branchial heart pressures. Each branchial heart discharges into an afferent branchial vessel, running along the base of the gill. Since there is no valve at the exit from the branchial heart^{47,51} pressures in the afferent vessel are the same as those in the heart.

Figure 3 shows a typical record which switches from the dorsal aorta to a branchial heart in mid-record. It can be seen, that the branchial heartbeat pressure is only about

one fifth of that of the ventricle, and that the two beat at the same frequency. The one to one relationship, between the beat of the systemic and branchial hearts, is maintained over a wide range of frequencies and pressures.

If pharmacological agents are injected into the afferent branchial vessels there is a delay of several beats before the effect on the systemic heart is detectable at the aortic level⁶². This suggests that the blood takes more than one beat cycle to pass through the gills with an active volume of 1.5–2 ml · kg⁻¹ between the branchial heart and ventricle. The total blood volume, both active and stationary, between the branchial hearts and the ventricle is not known, but estimates indicate a volume equivalent to 30–50% of gill weight (2.8 ml in a 1-kg animal; Clare Eno, pers. comm).

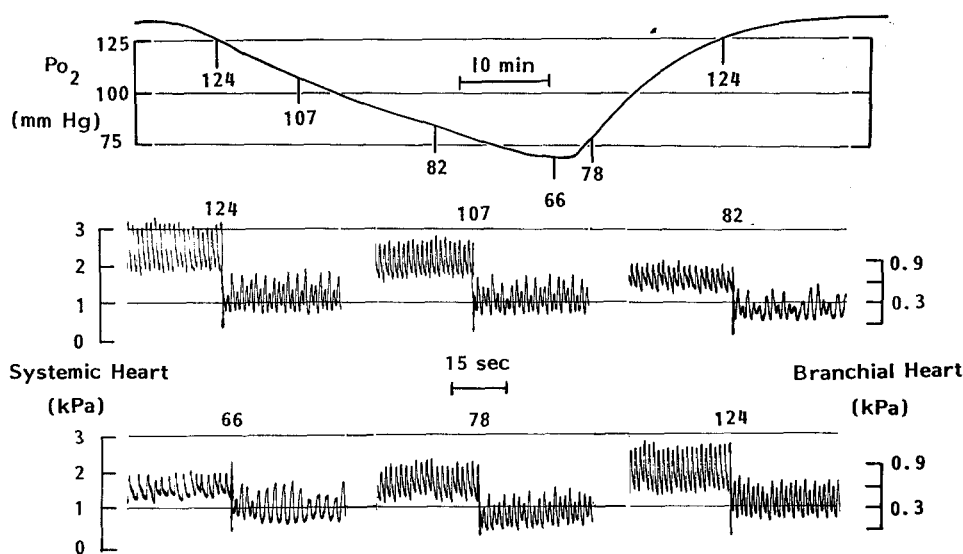


Figure 3. Systemic and branchial heart pressure pulses recorded from the dorsal aorta and afferent branchial vessel. In this experiment the animal depleted the oxygen in a closed respirometer until the PO_2 had fallen to 66 mm Hg. Circulation was then restored. Records show the systemic and branchial heartbeats at PO_2 's of 124, 107, 82 and 66 mmHg, and at 78 and

124 mmHg in recovery. Acute hypoxia slows and reduces both pulses, but the 1:1 relation is preserved and branchial heart pressures remain at around 20% of the systemic pressures throughout (from Wells and Wells⁶⁷).

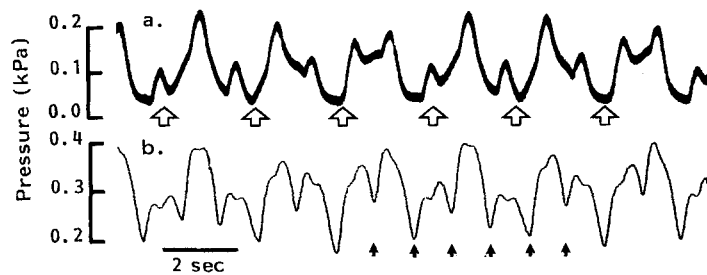


Figure 4. Pressure pulses recorded simultaneously in the efferent branchial vessel (a) and in the afferent branchial vessel (b). The onset of mantle contraction (recorded visually) is shown by the open arrows, with

closed arrows indicating the branchial heart contraction. Note how the more complex patterns repeat as the different cycles interact.

Efferent branchial vessel pressures. Pressure pulse records from the efferent branchial vessel of *O. dofleini* show two superimposed rhythms, the slower, and larger, of which coincides with mantle movements. Records from the smaller *O. vulgaris* show very similar wave forms in the efferent branchial vessel and atrium but the amplitudes are considerably lower (fig. 4). Johansen and Martin²³ suggest that the smaller, more rapid, pulses are due to gill movements and that the efferent branchials and the atria, into which they empty, play no significant role in the active propulsion of the blood. However, observations on lightly anaesthetised animals, with the mantle folded inside out, show contractions at the efferent branchial vessel to atrial junction, apparently linked to those of the branchial heart. At the moment we may still be underestimating the role of the efferent vessels in the regulation of flow.

Vena cava pressures. Both Johansen and Martin²³ and Smith⁴³ recorded pressure pulses in the vena cava cephalica (= anterior vena cava) of *O. dofleini* but found that these coincided with ventilatory movements, and concluded that no active contractions were demonstrable.

In *O. vulgaris*, and the lesser octopus *Eledone cirrhosa*, the lateral venae cavae are certainly contractile, with a pressure pulse of 0.2–0.3 kPa, more rapid and larger in magnitude than the pressure changes in the mantle cavity caused by ventilatory movements (fig. 5). The two pressure cycles interact, and since the blood vessels contract more frequently than the mantle, records of the type shown in figures 5 and 6 are common, as the two rhythms fall in and out of phase. The main pulse in a lateral vena cava proceeds at the same rate as the pulse in the afferent branchial vessel, but out of the phase with it, so that the peak pressure in the lateral vena cava precedes the larger branchial heart pulse (fig. 6).

Pressure pulses in the smaller veins. Mislin³¹ pointed out that the veins in the arms of the octopus were contractile,

with a tonal effect from the vasomotor centres reducing peristalsis to one half the uninhibited rate. Isolated lengths of arm vein will pulsate, and can be modulated by perfusion pressure³². Smith⁴³ working with *O. dofleini*, was able to record a rather irregular pulse of 0.1–0.3 kPa at this level, pumping blood from the arm veins into the cephalic veins, and from there into the anterior vena cava during the inspiration phase of mantle movements. All venous vessels, it seems, are contractile, with pressure gradually stepped up as the lateral venae cavae are approached; the role of the anterior vena cava alone appears to be passive⁴³.

2. Cardiac Output

Indirect measurement (Fick principle). Cardiac output can be estimated from the animals' oxygen uptake and the carrying capacity of the blood. The average, routine, oxygen consumption of 59 fasting *O. vulgaris* (371 ± 132 g) was found to be 53 ml · kg⁻¹ · h⁻¹⁶³. The oxygen carrying capacity of the blood has been measured as 3.4 ± 0.2 vols%, with a difference between the arterial and venous oxygen content, at rest, of 2.8%¹⁹. A Fick calculation, based on these figures, and allowing for 10% cutaneous uptake⁶⁷, gives a cardiac output of around 29 ml · kg⁻¹ · min⁻¹. Weight specific oxygen consumption declines with size, as weight^{-0.2} (*O. cyanea*)²⁹ so the cardiac output of a 1-kg animal can be estimated as 23 ml · kg⁻¹ · min⁻¹. These are *minimal* figures, since a recent meal, or activity (see below) can easily double the oxygen uptake. Feeding, in addition, has a relatively long-term effect on the routine rate; the oxygen consumption of 79 regularly fed, resting octopuses (355 ± 124 g) measured under the same conditions as those already considered, and 12 h or more after their last meal, was 76 ml · kg⁻¹ · h⁻¹. This is a 50% increase on the uptake of similar, fasting, animals^{63, 65}.

Direct measurement of flow. The flow of blood down the

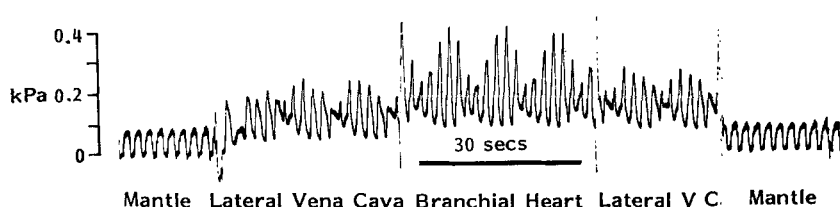


Figure 5. The internal mantle, lateral vena cava and afferent branchial pressures recorded from an octopus at rest. The three pressure bearing cannulae were switched successively into the same pressure transducer. This record shows: 1) That the branchial heart pulse has higher systolic and diastolic pressures than that in the lateral vena cava. 2) That these two

are at the same rate, here 0.58 Hz, and more rapid than the mantle pressure pulse, here 0.47 Hz. 3) That the BH pulse is half a beat out of phase with the LVC pulse and, 4) that the mantle pulse interacts with the faster blood pulses to produce cyclic fluctuations.

Table 2. Pressures in the aorta of freemoving *Octopus vulgaris*. Values show diastolic and systolic pressures in kPa* (and frequencies Hz) (extract from Wells et al.⁶¹)

Animal	Weight (g)	Recovery from anaesthetic (max)	At rest (min)	In exercise (max)	In recovery after exercise (max)
X12	2387	5–7 (0.87)	4–6 (0.83)	7–9.5 (0.81)	4–5 (0.88)
X26	1745	3.5–5.5 (0.71)	2.5–4 (0.62)	3–6 (0.58)	4.5–7 (0.57)
X46	1133	–	2–3 (0.67)	6–8 (0.68)	6–7.5 (0.60)
X40	1130	2.5–4 (0.60)	2–3.5 (0.70)	3.5–8 (0.67)	3–5.5 (0.72)
X42	755	4–6 (0.72)	2–4 (0.62)	4–8 (0.68)	3.5–6 (0.67)

* Values maintained for periods of several (usually 10–20) beats; very high transient values are found in jetting, but last only for a beat or two and are ignored here.

dorsal aorta can be measured directly by inserting fixed magnetic flow meters into the aortae (downstream of the branches to the viscera: fig. 1) in free-moving, intact, animals. At rest, the measured flow to the head and arms of 6 animals, averaging 1753 g, was $34 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (table 1). Fick calculations, based on the total oxygen uptake of the same animals, would predict a somewhat higher bloodflow of $49 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. This suggests that about two thirds of the cardiac output goes to the head and arms. The rest will go to the reproductive organs (the animals tested were mature males), to the coronary circulation, to the guts and to the mantle. Oxygen uptakes in these large animals were higher than expected (82 versus $50 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) almost certainly because of stress caused by the presence of the flow probes. Direct flow measurements from the aortae of *O. dofleini* using electromagnetic flow probes⁴¹ yield similar results, with stroke volumes 10–30% smaller than calculated by the Fick principle²¹.

The response of the circulatory system to stress

1. Acute hypoxia

Octopus regulates its oxygen uptake very successfully down to an ambient PO_2 of 70 mm Hg or less. As the oxygen declines, ventilation stroke volume and frequency both rise⁶⁸. Blood flow does not increase⁶⁹ (see also fig. 3), which implies that the quantity of oxygen delivered to the tissues, per unit volume of blood, remains the same despite the fall in environmental PO_2 . Since there is little or no scope for increasing the arterio-venous oxygen content difference (over 80% of the oxygen carried is removed even at rest¹⁹), the blood leaving the gills must still be fully saturated with oxygen. This rather surprising conclusion, is borne out by studies of the blood physiolo-

gy. The pH of the venous blood increases in hypoxia, so that the haemocyanin oxygen affinity increases. Loading at the gills is made easier, at the cost, presumably, of a lower PO_2 at the tissues¹⁹. Johansen, Brix and Lykkeboe²² found a similar result with *Sepia officinalis*.

So far as the cardiac output is concerned, acute hypoxia does not, therefore, present a problem. Down to as low as 50% saturation, the stress is dealt with almost entirely by changing the properties of the blood⁶⁹.

2. Exercise

Cardiac output. *Octopus* has a well-developed optomotor response, and will run in an exercise wheel at a speed of around $0.34 \text{ km} \cdot \text{h}^{-1}$ in order to keep its visual world steady. At this rate, which is about as fast as it can manage without swimming, animals, with a mean weight of 793 g, consumed an average of $150 \text{ ml O}_2 \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ ⁶⁴. The routine metabolic rate of the same group of animals, was $64 \text{ ml O}_2 \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$. Oxygen extraction from the blood hardly changes between exercise and rest²⁰; indeed, short periods of activity (10–20 s) can cause a drop in the PO_2 of post-branchial blood⁵² (Erratum: in this reference, the minute scale in fig. 4 is an order of magnitude too large). The $2.3 \times$ increase in oxygen uptake must be reflected in an almost equal increase in cardiac output. Similar results were found when flow was measured directly at rest, in exercise, and in two circumstances (after exercise and after anaesthesia) where oxygen uptake was elevated by the need to pay off an accumulated oxygen debt (tables 1 and 2). Since heartbeat frequency increases little or not at all under these conditions (indeed, it may even fall; see tables 1 and 2) practically the whole of the increased cardiac output must be met by increases in the stroke volume of the hearts.

Table 3.*

Animal	Branchial heart	Ventricle	Ventricle + 2 × branchial heart
Octopods			
<i>Octopus vulgaris</i> **	0.11	0.09	0.31
<i>Octopus dofleini</i> ³⁰	0.16	0.12	0.46
<i>Eledone cirrhosa</i> ⁸	0.165	0.14	0.47
Decapods			
<i>Rossia pacifica</i> ³⁰	0.076	0.173	0.31
<i>Architeuthis giganteus</i> ³⁰	0.071	0.165	0.31
<i>Illex illecebrosus</i> ³⁰	0.212	0.299	0.67
Teleosts (ventricle only)³⁷			
Tubular (eg. Ling & Hake)		0.054	
Sac-like (eg. Dab & Cod)		0.035	
Pyramidal (eg. Herring)		0.167	

* (Heart weight ÷ body weight) × 100; branchial heart weights include the non-contractile glandular tissue, comprising the bulk of the volume;

** M. J. Wells, unpublished.

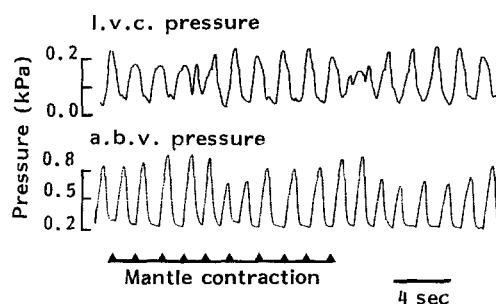


Figure 6. Simultaneous pressure recordings from the lateral vena cava (upper trace) and the afferent branchial vessel (lower trace) on the same side from *Octopus vulgaris*. The timing of the mantle contraction was manually recorded by visual observation. The pressure record from the l.v.c. is complicated by its interaction with the pressure generated during mantle contraction.

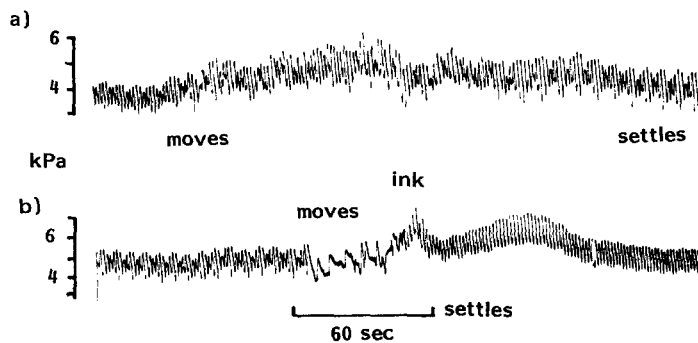


Figure 7. Blood pressure and movement. a) Shows pulse changes in the dorsal aorta during a period of slow walking. In b) the animal was stimulated to move by placing a white bucket lid in the tank and moving it towards the octopus. The effect of this was to cause the animal to crouch down and to blow jets (once with ink) towards the object, as it moved

away. These activities interrupted the blood flow and were followed by a period of increased pulse as the animal settled down, presumably associated with repayment of a metabolic debt run up during the period of reduced circulation (from Wells et al.⁶¹).

Stroke volumes can be estimated from Fick calculations, or derived directly from flow measurements where the frequency and minute outputs are known. In the case of the exercise wheel experiments, the Fick calculated stroke volume rose from $0.8 \text{ ml} \cdot \text{kg}^{-1}$ to $1.8 \text{ ml} \cdot \text{kg}^{-1}$, a 2.3-fold increase. Direct flow measurements indicate a slightly smaller increase, averaging $1.8 \times$ (table 1) but the animals were not moving as rapidly (average 0.17 as opposed to $0.34 \text{ km} \cdot \text{h}^{-1}$) and in these cases, the oxygen uptake was already elevated at rest, due, perhaps, to the presence of the flow transducers.

Blood pressures. In exercise, aortic pressure is enhanced considerably. Systolic pressures in excess of 10 kPa are quite common, and there are corresponding increases in the diastolic pressures⁶¹. Very high pressures are associated with jet propulsion, but even walking, at a gentle pace, can almost double the blood pressure (fig. 7a and table 2). Large pressure pulses are also found after exercise and during recovery from anaesthesia. The exercise after-effect is particularly marked if the animals have been moving by jet propulsion, which seems to interfere with the normal blood flow (figs 7b and 8). In both cases the apparent extra flow is associated with repayment of an oxygen debt.

Additional oxygen demand increases the branchial heartbeat pressure, as it does the systemic, with systolic pressures rising to a maximum of 1.0 – 1.2 kPa ; there is a corresponding increase in diastolic pressure to 0.3 – 0.4 kPa ⁵⁹.

The contrast between the mammalian solution to increased oxygen demand during light exercise, and that of

the octopus is well illustrated by the ventricular work-loops (fig. 9)⁴⁸. These show not only the stroke volume changes, but also the increase in the pressure at which ejection from the ventricle occurs. In man, despite an elevated oxygen demand of 5–6 times, the work-loop area increases in exercise by only about 30%, compared to 5 times for the octopus. The difference in the mammal is partly due to increasing the heart rate but, even when this is taken into account, the octopus has still to increase the ventricular power output in exercise by 7 times, compared to a human value of 2.5 times.

Control of the circulation

Within the Mollusca the cardiovascular system of the cephalopods is uniquely complex. There are several sites of rhythmic pressure generation and therefore several possibilities for the pacemaker or pacemakers controlling the blood flow. Very basic questions arise. How are the contractile vessels and organs coordinated? What regulates their level of performance? The answer to the first of these questions is frustrated by the difficulty of developing physiological preparations that behave realistically in vitro, and the answer to the second by a past preoccupation with changes in heart rate or with the force of contraction, the latter measured in a way that we cannot easily relate to the in vivo condition. As we have shown in this review, heart rate is now recognised as largely irrelevant in *Octopus* in vivo.

1. Isolated organs

The ventricle. The output of a contractile organ can be governed by two separate but functionally interactive control systems. The first, intrinsic control, is based on the properties of the myocardium and the second, extrinsic control, on the influence of the nervous system. Studies on the isolated ventricle of *Eledone cirrhosa*⁴⁵ show that this organ obeys Starling's law, with a responsive stroke volume and a mainly stable heart rate. A greater sensitivity in heart rate might occur at lower pressures, as in some other molluscs⁴⁹ but this has still to be examined in detail. These conclusions also apply to the isolated ventricle of *Octopus vulgaris*¹². Both these cephalopod studies, however, suffer from the defect that atrial perfusion levels were set according to values measured from *O. dofleini*²³. Subsequent work has shown these values to

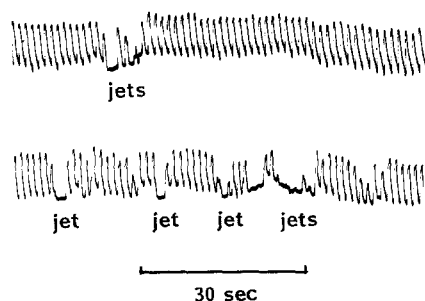


Figure 8. Blood flow and jet propulsion. Steady flow was interrupted when the animal produced propulsive jets in the course of movement.

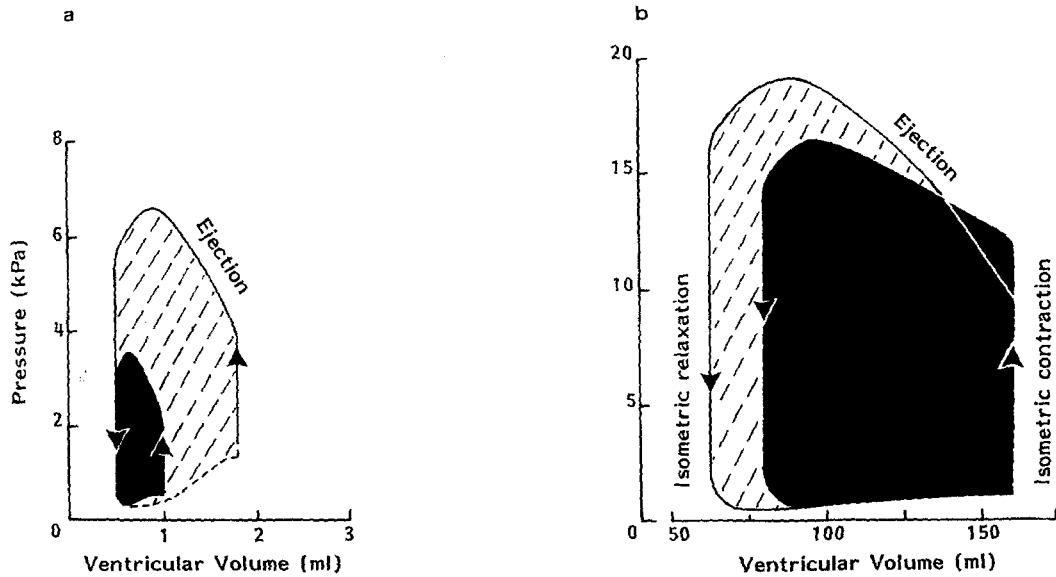


Figure 9. Ventricular work-loops for a 500-g *O. vulgaris* (a) and a man (b). The shaded areas are the resting loops and the hatched areas represent the changes that occur when the octopus walks or the man takes light exer-

cise. The coordinates of a work-loop are set by performance levels of pressure and stroke volume. The area of the loop is proportional to the stroke work (after Smith⁴⁸).

be an order of magnitude too high for the smaller *O. vulgaris* and presumably for *E. cirrhosa* as well (fig. 4)⁴⁸. At the atrial pressures actually found in the smaller species, the mechanical power output of the isolated octopod heart is far too low in comparison with the in vivo performance ($0.14 \times 10^{-3} \text{ W} \cdot \text{g}^{-1}$ versus $1.2 \times 10^{-3} \text{ W} \cdot \text{g}^{-1}$ ventricular tissue)^{48, 49}. Ventricular contraction is also unreliable at these pressures and frequently the organ is quiescent⁴⁵.

As yet, the reason for the poor performance of the ventricle in vitro is unclear. There are several possibilities. The most obvious is the complexity of the ventricular structure, particularly with regards to the coronary vasculature, indicating that the heart really has to be treated with the same care as a vertebrate heart with a compact myocardium. In addition, the hearts in both studies were removed from the renal sacs. These enclosing and closed volumes might significantly effect the filling conditions for the ventricle in vivo at low atrial pressures. It may also be that seawater is a poor perfusion medium, perhaps lacking the correct amino acid composition or gas bal-

ance¹¹. Another possibility, suggested by Smith⁵⁰ for molluscs in general, is that in vivo the hearts might be tonically regulated by circulating cardioactive neurohumours, such that the action of a humour could overlie, to a variable degree, the inherent myogenicity. Certainly in the cephalopods there is no lack of circulating cardioactive agents (see this review).

What is clear from the work on isolated ventricles, is that the organ is myogenic, having an inherent rhythmicity in isolation when sufficiently stretched by a returning preload level (0.2–0.6 kPa)^{14, 35, 42, 45}. Whether the contraction arises at a specific point in the myocardium is not yet clear. The organ does have a very clearly defined cardio-gram⁴⁶ suggesting a regulated contraction and several authors have noted a sensitivity of the ventricle in the atrio-ventricular junction region. It is likely that a pacemaker zone exists in this area. Certainly, in other molluscs this would seem to be the case²⁸ and the old concept of diffuse myogenicity is no longer appropriate.

The branchial hearts. One problem with working on the output of the isolated branchial heart of the octopus is

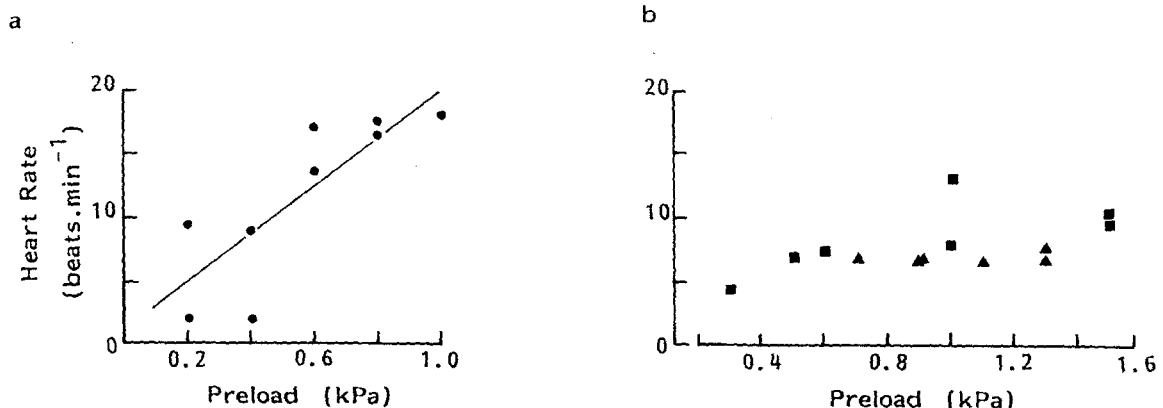


Figure 10. Response of the isolated and perfused branchial heart to changes in the preload perfusion pressure. In (a) the contraction rate is

significantly affected by changes in the pressure. In the preparations shown in (b) there is no obvious relationship (from Smith⁴⁴).

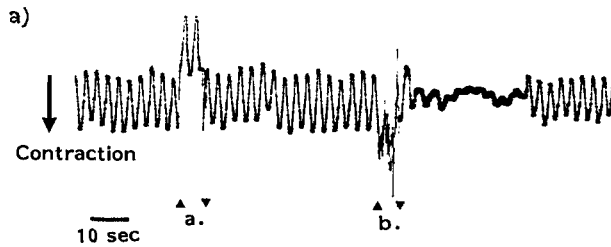
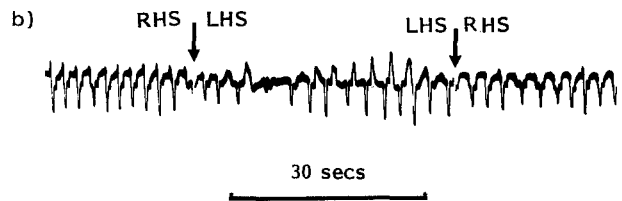


Figure 11. a) Contractions of the isolated and perfused branchial heart, during normal activity and after the application of a brass rod, cooled in liquid nitrogen, to the outer wall of the heart (a) and to the cardiac ganglion (b.). At (a) there is no effect on the rhythm. Freezing the ganglion stops the heart but activity returns as it thaws (from Smith⁴⁴). b) In vivo records from the right and left branchial hearts, after removal of the cardiac ganglion from the left side. Impedance records, switched



from the RHS to the LHS and back to the RHS during a continuous recording. The LHS beat is less regular, but where it occurs, it is at the same rate and approximately in phase with the RHS, presumably triggered by the simultaneous arrival of a pulse down the two limbs of the lateral vena cava; the rather slow beat, 0.4 Hz, is due to the low temperature, here 15 °C (from Wells⁵⁸).

the lack of a valve at the junction with the afferent branchial vessel. Stroke volume measurements can be made in vitro by transplanting the atrio-ventricular valve from the systemic heart, to the output cannula⁴⁷. The performance of the heart at low pressures is better than that of the ventricle, with stroke volumes from the individual organs of around $0.3 \text{ ml} \cdot \text{kg}^{-1}$ (*E. cirrhosa* at 10 °C) but the preparations are still unreliable. The response of the heartbeat frequency to variation in preload levels is not nearly as constant as for the systemic heart (fig. 10)^{44,45} and is slower than would be expected from in vivo studies⁴⁷. Myogenicity is clear for the ventricle but the same cannot be said for the branchial heart. The cardiac ganglia, with their unique, and as yet functionally unexplained, pulsating sacs, are an integral part of the branchial hearts¹ and several studies have shown that the ablation of the ganglion, in vitro, stops the contraction of the ipsilateral

heart (fig. 11a)^{35,44}. On this basis it would appear that the branchial heart is neurogenic, making it the only such case known in the Mollusca. In vivo, however, ablation of the ganglion does not permanently disrupt the heartbeat and the branchial heart is found capable of contracting, in the absence of the cardiac ganglion, when rhythmically stretched by a pulsatile preload from the lateral venae cavae (fig. 11b).

The branchial heart is clearly a well-vascularised structure (fig. 12); it is unlikely that it operates anaerobically as has sometimes been assumed in the past¹¹.

The gills. The cephalopod gills remain one of the least understood areas of the cardiovascular system. This is a major liability when trying to understand the performance of the system, as these organs are central to many of the problems we have considered in this review. Observations of the gills in lightly anaesthetised animals show the lamellae to be contractile. Blood within the lamellae tends to accumulate at the efferent end if the flow is strangulated at each end in vivo (Clare Eno, pers. comm.). Isolated and perfused gills also contract regularly (B. K. Evans and P. Darling, in prep.). Taken together, this evidence implies active peristaltic propulsion of the blood through the gills.

Unlike the situation in fish, there appears to be no bypass through which the blood can follow a low-resistance path when oxygen demand is low (B. K. Evans and P. Darling, in prep.). There is, on the other hand, evidence that the total blood content of the gills rises in times of high oxygen demand, which would indicate some expansion of existing pathways or the recruitment of additional vessels (Clare Eno, pers. comm.).

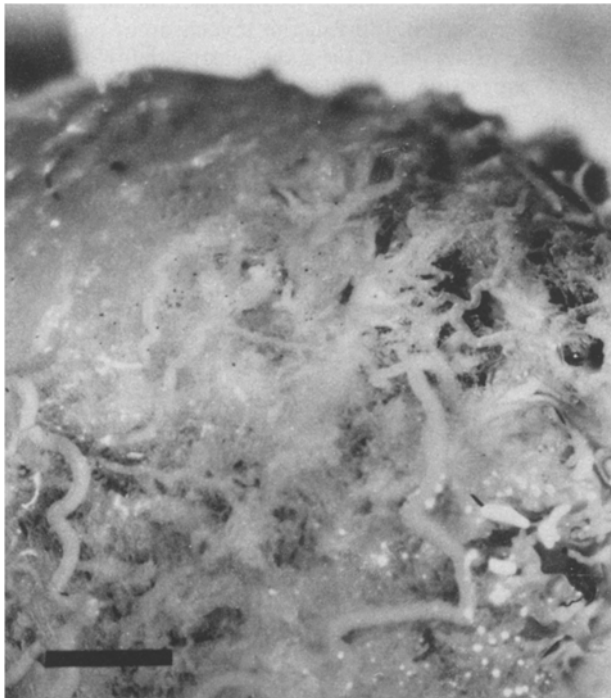


Figure 12. Arterial vessels running to the outer muscular rind of a branchial heart, revealed by injecting the abdominal aorta with a low viscosity resin and removing the soft tissues with 1M KOH. The scale bar is equal to 100 μm .

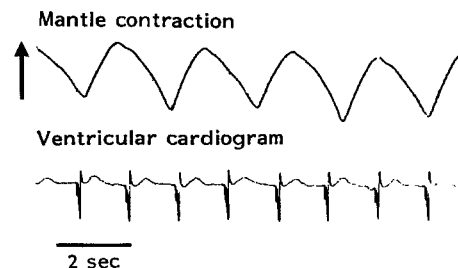


Figure 13. Simultaneous recording of the mantle contraction (impedance recording) and the ventricular cardiogram from a free-moving *O. vulgaris*. There is no obvious relationship between these events.

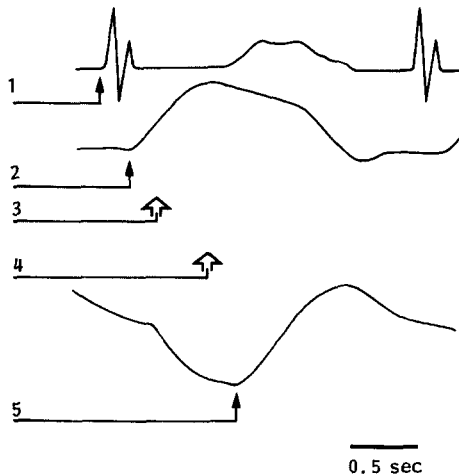


Figure 14. Summary of the contraction sequence for the cardiac organs of an octopus (from Smith⁴⁴). 1, Ventricular cardiogram; 2, Onset of ventricular contraction; 3, Contraction of the lateral venae cavae; 4, Contraction of the intraganglionic body in the cardiac ganglion; (placed approximately, relative to intervals 3 and 5); 5, Onset of branchial heart contraction.

2. Intact and semi-intact physiological preparations

Despite the contribution that Ransom³⁵ made to our understanding of the cardiac rhythmicity in the octopus, his intact preparation is not to be recommended today, except to those with the most sadistic tendencies. An octopus will live, nailed to a board with its mantle split open, but the conditions must be stressful. Erroneous conclusions can result, such as the 1:1 linkage of ventricular and ventilatory contraction rates, now clearly shown to be incorrect (fig. 13). A better approach is to develop a semi-intact preparation, as done by Fry¹⁴, Fredericq and Bacq¹³ and Kruta²⁷. These studies were principally concerned with visceral nerve stimulation and not with organ linkage. They have been reviewed before¹⁸ and will not be dealt with here, partly as the emphasis throughout is on heartbeat frequency changes.

Smith⁴⁴ began the development of a semi-intact preparation where both the anterior vena cava and the efferent branchial vessels could be perfused separately. The double cannulation was necessary as the gills, in these preparations, formed an insurmountable resistance to flow. Although still far from perfect, this preparation shows the following features: as in vivo the contraction sequence is, the ventricle, followed quickly by the lateral

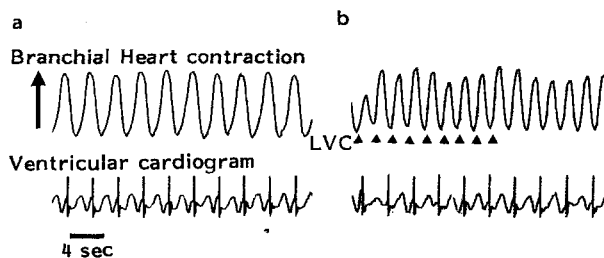


Figure 15. a) Simultaneous recording of branchial heart contraction (upper trace) and the ventricular cardiogram (lower trace) from a semi-intact physiological preparation. The nerves between the two organs were intact but the l.v.c. was contracting as in b), more rapidly than the branchial and systemic hearts. b) As in a) but after the visceral nerve connecting the ventricle and the branchial heart was severed. Now the branchial rhythm follows that of the lateral venae cavae. (After Smith⁴⁴).

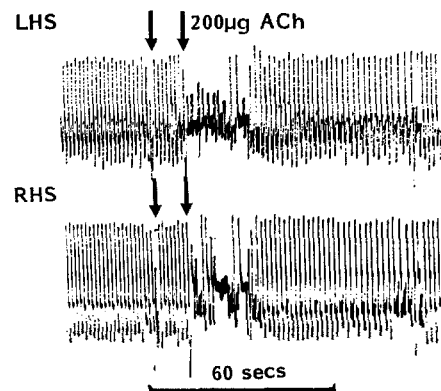


Figure 16. Impedance records of branchial heartbeats, recorded simultaneously on the two sides of the animal. 200 µg ACh was injected into the LHS branchial heart during the period shown by the arrows. The effect was at once mirrored in the RHS branchial heart (from Wells⁵⁸).

venae cavae and then the branchial hearts. Branchial heart contraction is preceded by the contraction of the sacs in the two cardiac ganglia (summarised, along with the in vivo data, in fig. 14). Normally the relationship between these contractile components is 1 to 1. Sometimes, however, the venae cavae fall out of synchrony with the ventricle. The branchial hearts will still follow the ventricle until the visceral nerves, distal to the fusiform ganglia, are cut. The branchials then follow the rhythm of the lateral venae cavae (fig. 15).

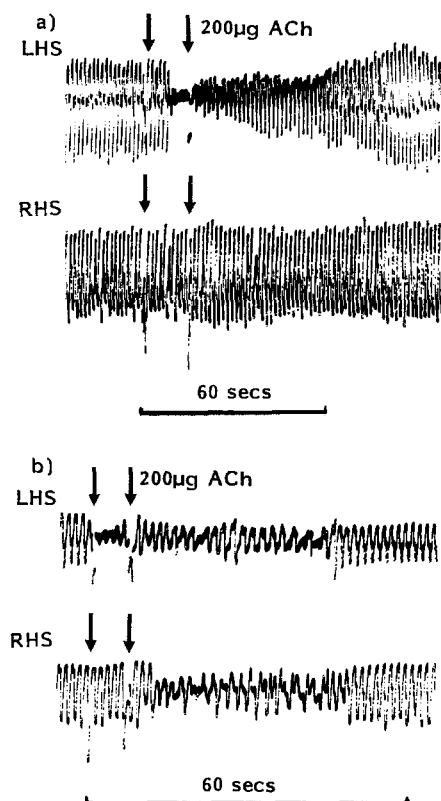


Figure 17. Impedance records, as in figure 16, but after severance of the connective joining the cardiac and fusiform ganglia on the RHS. In a) the message was no longer relayed from LHS to RHS. In b), made later with the same animal, an effect was found, but only after a delay of 8 or 9 beats. The most probable explanation is that the drug now passed to the contralateral heart via the coronary circulation (from Wells⁵⁸).

Nervous control of the blood flow through the hearts in vivo

Early attempts to disrupt performance of the cardiac organs, by removing elements of the visceral nervous system, soon showed that the system is remarkably resistant to damage. Cutting the visceral nerves has no visible effect on the resting heart rate, although there is some evidence that the operation may interfere with the response to stress in exercise; the blood pressure pulse tends to die away, rather than augment, when such animals are handled⁵⁸. However, this has not been well characterised. After nerve section the response to temperature and to acute hypoxia also remain as in the intact animal⁵⁸. These last results are not surprising, since temperature presumably acts directly on the inherent rhythmicity of the myocardium and, as explained above, the adaption to hypoxia is to be found in the physiology of the blood.

Cutting the nervous link between the cardiac ganglia through the fusiform ganglia stops direct communication between the two branchial hearts via the nervous system. The two normally beat in phase. Agents, such as 5-hydroxytryptamine and acetylcholine, injected into one, have effects that are at once mirrored in the other (fig. 16). Cutting the nervous link prevents or delays the response in the non-injected heart (fig. 17): a delayed response is possible because the injected agents will eventually reach the contralateral branchial heart through the branchial heart coronary circulation, stemming from the ventricular abdominal artery (fig. 2 and fig. 12).

The immediate effect of removal of a cardiac ganglion is to seriously upset the branchial heartbeat on that side. Blood pressure in the aorta falls, as the blood supply to the systemic heart is reduced. The animal can, however, survive the removal of both cardiac ganglia, and a regular coordinated heartbeat, with normal pressures, is generally re-established⁵⁸. How is this achieved? The probable explanation lies in the discovery of an extensive nerve supply to the lateral venae cavae, arising from the ventral

surface of the ventricle and its associated nerves (fig. 8)^{45,51}. If contraction of the ventricle were to trigger the contraction of the lateral venae cavae in vivo, as in vitro preparations imply⁴⁴, and if this were subsequently to stretch the branchial hearts inducing contraction, a coordinated response would continue after denervation (as in fig. 15).

Cutting the small nerves from the ventricle to the venae cavae is technically difficult. Successful operations seem to have a drastic effect on the ventricular beat interval, apparently because they disrupt the regular contraction of the lateral venae cavae. This in turn disrupts the beating of the branchial hearts and the blood supply, through the gills, to the systemic heart⁴⁵. In extreme cases the ventricle can show what is apparently paroxysmal tachycardia⁴⁶.

In the normal course of events the renal sacs may perform a role akin to that of the constant-volume pericardium in other molluscs, where contraction of the ventricle sucks blood into the atrium or atria. The cephalopod ventricle, its atria, and the lateral venae cavae are all enveloped in the renal sacs, so the contraction of the ventricle may assist in the filling of the thin-walled vessels. The nervous link between the ventricle and the lateral venae cavae evidently controls the timing of the subsequent contraction.

The material discussed above implies that the ventricle is the pacemaker for the system. An alternative view, that the pacemakers for the beat rhythm lie in the cardiac ganglia, arises, a) from the immediate effect of their removal, b) from the existence of a pulsating sac in each ganglion¹ and c) from the abundant in vitro and in vivo evidence which seems to show that the ventricle only contracts when it is filled^{58,59}. Indeed, this last sort of evidence led Skramlik⁴² to conclude that the automatism of the hearts is purely initiated by internal pressure effects, a view at odds with Ransom³⁵ who felt that although internal pressure is essential, it does not replace

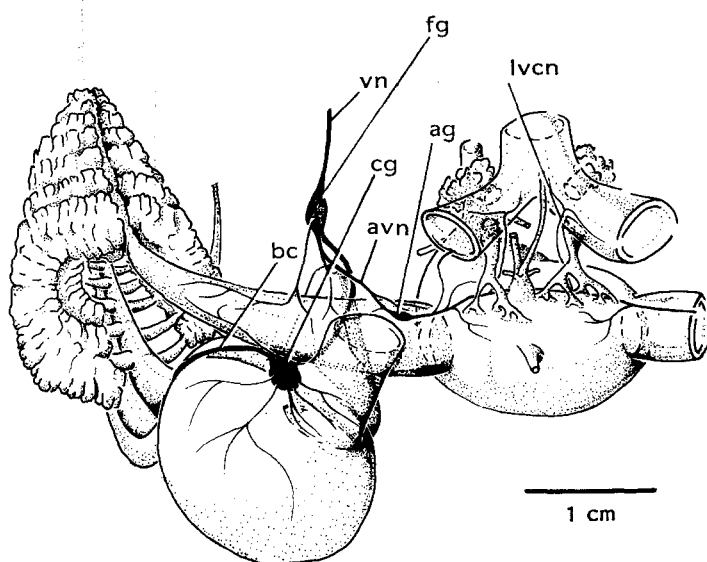


Figure 18. Summary of the innervation to the ventricle and associated organs and vessels in the lesser octopus, *Eledone cirrhosa*. The preparation is viewed from the ventral surface, simplified and shows the right side only. Nerves to the renal papilla, gonoduct and sections of the lateral vena

cava are omitted. With the exception of the atrial ganglion, the innervation is bisymmetrical; ag, atrial ganglion; bc, branchial connective; avn, atrial-ventricular nerve; cg, cardiac ganglion; fg, fusiform ganglion; lvcn, lateral vena cava nerve; vn, visceral nerve. (after Smith and Boyle⁵¹).

the intrinsic automatism. On balance, work by Ransom³⁵, Smith⁴⁴ and Smith and Boyle⁵¹ indicate that the ventricle leads the contraction sequence. There is strong, indirect, evidence which supports this. In acute hypoxia the heart rate slows, but the interval between the systemic and branchial heart contraction does not; the same applies to small spontaneous changes in the normal heartbeat rate (fig. 19)⁴⁴. Changes in heart rate are taken up by changing the interval between the contraction of the branchial heart and the ventricle. The suggestion is that the ventricle leads the contraction cycle, providing a common reference point for the other pacemakers, with its contraction interval being determined by haemodynamic parameters, which are themselves set by the performance of the other contractile elements⁵¹.

It must be remembered, moreover, that there are hormonal controls. In many molluscs the cardiovascular system is considered open (see Jones²⁴ for a discussion of this point) and therefore the blood volumes are large. The dibranchiate cephalopods have a closed system, with a blood volume of about 3.6% of the body weight, and a circulation time of around 60 s (40–70 beats)³⁴. Circulating cardioactive substances could, therefore, be used for the relatively rapid modulation of cardiac performance. Materials produced from extensive neurosecretory areas in the anterior vena cava alter cardiac performance when injected at the level of the branchial hearts^{60,62}. These areas are innervated directly from the brain^{2,3}. Further details of hormonal effects on the hearts are given elsewhere in this review.

Manipulation of the stroke volume: The role of the nervous system

In *Octopus*, the ventricle responds to stretch as expected from Starling's law of the heart⁴⁵. However, unlike the mammalian ventricle, the stroke volume changes considerably in response to a varying oxygen demand^{48,61}. To achieve this, it is inevitable that the myocardial response to preload must vary. Unfortunately, none of the work discussed above addresses the problem of how stroke volume is controlled. Such work must wait until a reliable in vitro preparation, with performance levels approximating to those found in vivo, is available. Volume regulation must depend in part on the regulation of myocardial tone. This has been considered by Smith⁵⁰ in a review of molluscs generally. In the gastropod *Busycon*, acetylcholine increases the end-diastolic volume for the same returning venous pressure⁵⁴ whereas 5-hydroxytryptamine, and the tetrapeptide FMRFamide, reduce it^{53,54}. A balance of the action of these cardioactive substances could regulate stroke volume in cephalopods but more research is still needed.

Conclusion

The struggle to develop a high performance system from a fundamentally unsuitable design

The basic design of the molluscan circulatory system was laid down long before large active members of the group emerged. It is well suited to a slow-moving animal with a hydrostatic skeleton, but a disaster for large, high-metabolic

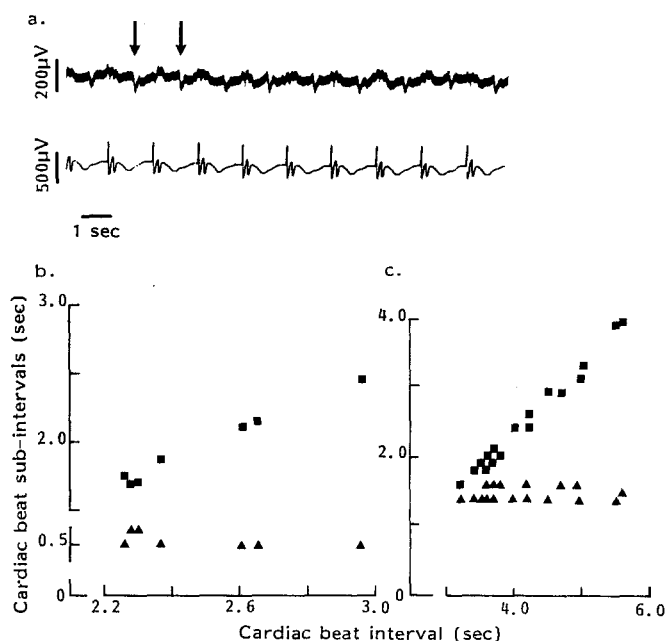


Figure 19. a) Simultaneous electrical recordings from the branchial heart (upper trace) and the ventricle (lower trace) of a free-moving *O. vulgaris*. The arrows indicate the moment of branchial heart depolarization. A weak ventricular electrocardiogram can be seen in the upper trace, recorded from the branchial heart. b) The relationship between the intervals separating the electrical events shown in a). The triangles represent the times between activity in the ventricle and the next event recorded

from the branchial heart, whereas the squares give a measure of the following interval, between the branchial heart and the ventricular cardiogram. c) As in a) but for recordings made from an *Eledone cirrhosa* undergoing a period of hypoxia. This slows the heart rate. The relationship described in b) remains over this extended range of variability (all records from Smith⁴⁴).

bolic rate invertebrates, competing with fish and other vertebrates. Natural selection works on the material available, and the cephalopod circulatory system is a miracle of making the best of a bad lot. The many pumps, the detailed innervation, and the size of the hearts, particularly in the more active species (table 3), all underline a struggle to support an aerobic metabolism which makes its largest demands on the blood supply when muscle contraction makes it maximally difficult to deliver the goods.

In *Octopus* the system fails at the highest levels of normal activity. The animal seems unable to deliver blood when using vigorous jet propulsion, perhaps because pressure in the mantle interrupts the venous return to the great veins from the head and arms. The animal must, inevitably, work on oxygen debt at these times⁶¹. In the life of *Octopus vulgaris*, jet propulsion probably plays a minor role. Animals undoubtedly use it to move from place to place in their environment but only for a few seconds at a time, a situation that will pose no problem, even with the very limited oxygen debt that *Octopus* is able to sustain. Normal exploration and food gathering is done at a walk and in this situation we know that the animal can remain in oxygen balance for at least two hours⁶⁴. This is, probably, comfortably in excess of any likely demand, since there is no indication that these animals regularly migrate for long distances.

With squid the situation must be different. For example, the sustainable maximum swimming speed for a 400-g *Illex illecebrosus* is around 75 cm·s⁻¹. At this rate the fins are folded against the body and play no part in propulsion, which is entirely by jetting. Average mantle pressures during jetting are in the region of 0.43–0.63 kPa⁵⁶. We have no reliable figures for pressures in the great veins of a squid. Bourne recorded from the anterior vena cava of *Loligo pealei*, but found that the major component of the pulse coincided with ventilation. More frequent small pulses, superimposed on this, were of the same magnitude as the pressure pulses in the great veins of *Octopus* (0.2–0.3 kPa in systole; see fig. 5), which would seem quite inadequate to drive the blood from the head and arms into the mantle against the pressures generated during jet propulsion. It should, on the other hand, be noted that the situation in squid is different from that of the octopus in a number of ways. Most of the blood in the squid goes to the mantle, and from here it is not obliged to return along an uphill pressure gradient to reach the vessels within the mantle cavity. Further, the muscles of a jetting squid are extended partly by elastic recoil of the connective tissue tunics¹⁶ and this would tend to draw blood into the relaxing muscle.

Squid, indeed, are the place to look for a demonstration of what can really be achieved with the molluscan system. The fact that at present we have information only for exercising *Octopus* is a reflection of the technology of monitoring performance in vivo. Squid are difficult laboratory animals, require much space and are readily damaged, so that information, even about oxygen uptake in exercise (let alone the circulatory adjustments occurring), is only just becoming available^{33, 56}. The metabolic rate of a swimming squid is impressive, over 1000 ml·kg⁻¹·h⁻¹ for a 400-g *Illex*, almost seven times that of

Octopus vulgaris and twice the metabolic rate of a salmon of comparable size^{9, 56}.

Very high metabolic rates arise because a cephalopod must resort to jet propulsion to swim at all rapidly. Jet propulsion is inescapably expensive, as a relatively small volume of water must be accelerated to a high speed, and ejected in pulses. It costs a squid, such as *Illex*, something like twice as much energy, to travel half as fast, as a salmon. The difference would be even more extreme if comparisons were made with mackerel or tuna, which hardly flex the body. They swim even more efficiently by oscillations of the caudal fin⁵⁶. Add to these problems the appallingly low carrying capacity of cephalopod blood, and it is evident that the circulatory pumps must be achieving something rather remarkable in terms of cardiac output. An active *Illex*, with an assumed arterio-venous oxygen content difference of 3.8 vols%, must pump over 400 ml·kg⁻¹ of blood per minute. We have no figures for the active heartbeat rate of a squid, but even if we assume that it increases by as much as 50% (exceeding anything found in the *Octopus*) from a resting value of 1.7 Hz (100 g *Loligo*)⁵, the stroke volume must reach 2.6 ml·kg⁻¹, an almost incredible output from a heart weighing only 3 g·kg⁻¹.

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