Millar considers that there is a "pattern of reversal inherent in the heart", but admits that periodic pressure changes may, of course, influence the behaviour of the heart in the intact animal. The regularity of the reversals in the intact animal and the experimental fit to the theoretical that we obtained, as opposed to the wide variations in times between reversals in the isolated heart, are very strong evidence that back-pressure is the controlling mechanism in the intact animal to an overriding extent. In other words, there are two stable modes of action of the heart—abvisceral and advisceral—and back-pressure is the mechanism causing the limitation of one mode in the intact animal. How the transition to the other mode takes place is no concern of the theory. It seems almost certainly to be bound up in some way with the capacity of each end of the heart to initiate contractions. In an isolated and therefore abnormal heart, the beats one way might well be expected to fail to dominate the other consistently, especially when the heart is almost moribund.

We have recently repeated Millar's experiments but did not observe reversal in the isolated hearts of four specimens of *Ciona intestinalis* even after ten hours. However, in two specimens, by merely touching the appropriate end of the heart, reversal could be made to take place at will. In one of the cases the beat continued in the reversed direction, whereas in the other case the reversal was only temporary. It is difficult to know to what extent conclusions can be drawn at all from experiments on hearts not *in situ*, but this is certainly in favour of the idea of two stable modes of action. When reversals occur in the isolated heart without direct mechanical stimulus it could well be due to a variety of causes: local variations in temperature, metabolism, progressive fatigue, weakness of the mechanism controlling the dominance of one mode, etc. It is not, however, valid to conclude that the back-pressure theory is untenable. In fact it seems to us that an "inherent pattern of reversal" can have no significance at all unless it be a *regular* pattern in some way. A mere alternation between the two available directions of beat in circumstances which preclude back-pressure phenomena is insufficient evidence to disprove a verified quantitative theory of the regularity of reversal in the intact animal.

We would stress the need not only for a very thorough re-investigation of the peculiar muscle cells of the Tunicate heart but also the need for definite evidence as to whether the heart is myogenic or neurogenic, before any *complete* theory of the reversal phenomena can be formulated.

C. A. Haywood
H. P. Moon

University College, Leicester.
Jan. 6.

[1] Haywood, C. A., and Moon, H. P., *J. Exp. Biol.*, **27**, 14 (1950).
[2] Lahille, "Contributions à l'étude anatomique et taxonomique des Tuniciers" (Toulouse, 1890).
[3] Millar, R. H., *Nature*, **170**, 851 (1952).

In the above communication, Haywood and Moon stress the irregularity of reversal in the isolated hearts in my experiments, and suggest that the reversal of these hearts is due to their abnormal condition, or to random variations in their environment. It seems to me that the fundamental behaviour of these hearts is their repeated reversal and that it is the irregularity which is more likely to be an abnormality.

However, the most important aspect of the whole question has, I think, been adequately dealt with by von Skramlik[1] in a very important paper which was not referred to in Haywood and Moon's (1950) original contribution. Von Skramlik not only followed the repeated reversal of isolated hearts of *Ciona intestinalis* (after an initial period of one-way beating), but also—and this seems very important—he located a controlling centre at each end of the heart, isolated each of these two centres, and found that each had a rhythmically changing pattern of beating (see von Skramlik, p. 622, Abb. 6), in which series of beats and short pauses alternated. After each pause the isolated controlling centre restarted beating slowly before acquiring its full rate. This activity of the controlling centres is precisely the basis of the "pattern of reversal inherent in the heart" to which I referred in my letter to *Nature*. The heart, therefore, it seems to me, possesses its own mechanism for periodically stopping and reversing, however the action of this mechanism is modified by blood pressure in the intact animal.

A number of other points may also be made in connexion with Haywood and Moon's (1950) paper. They state (p. 15) that "A modified form of the back pressure theory has been put forward by von Skramlik (1930) in which reversal is associated with the periodic contraction of the whole animal, bringing about a reduction of the capacity of the blood vessels by constriction, thus facilitating a build-up of back pressure and subsequent reversal". This statement does not give von Skramlik's view of the activity of the ascidian heart, and in the experiments reported by him (1930) there was no question of "periodic contraction of the whole animal". The contractions in question followed stimulation applied by the experimenter. Von Skramlik states that in the normal, relaxed state of the animal it is the rhythmically varying frequency of beating of the two controlling centres that is responsible for reversal.

Enriques (1904), in stating that there is merely an oscillation of blood to and fro in the vessels, was later proved to be wrong by von Skramlik (1929), who demonstrated a true circulation. Indeed, it is difficult to see what fundamental difference there is in the ascidian blood vessels, as opposed to the system of many other animals possessing a true circulation, which necessitates the application of a theory of back-pressure. But this is an aspect that I would not stress as it depends on measurement of the capacity of different parts of the blood system, which to my knowledge has not been made.

I agree that "It is difficult to know to what extent conclusions can be drawn at all from experiments on hearts not *in situ*", yet this technique has given useful experimental results in other animals. I believe that, when isolated hearts, albeit after an interval of one-way beating, behave in essentially the same way as do hearts *in situ*, and furthermore when an adequate functional basis (rhythmic variation in the controlling centres) is revealed, the conclusion is justified that the tunicate heart has its own inherent pattern of reversal.

R. H. Millar

Marine Station,
Keppel Pier,
Millport.

[1] *Z. vergl. Physiol.*, **4**, 607 (1926).