DIRECTIONAL DIFFERENCES IN THE CONDUCTION OF THE IMPULSE THROUGH HEART MUSCLE AND THEIR POSSIBLE RELATION TO EXTRASYSTOLIC AND FIBRILLARY CONTRACTIONS

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Heart muscle ordinarily conducts the wave of excitation with equal facility in either direction. This has seemed to be a necessary consequence of the myogenic theory which is now almost universally accepted. Nevertheless, it is well known that there may be differences in the duration of the pause at the auriculo-ventricular junction depending upon the direction of conduction, and that various forms of treatment of that region may variously affect the delay in the two directions, even to the extent of producing unidirectional block (Engelmann, 1894; Mines, 1914; Skramlik, 1920). Furthermore, it has been demonstrated that strips of heart muscle, apparently homogeneous, can be made to exhibit not only differences in conductivity depending upon the direction of the beat, but even unidirectional conductivity (Erlanger, 1906). The present experiments were carried out primarily in the hope of shedding some light on the conditions determining the development and the direction of such differences in conductivity.

The method employed has consisted, in principle, of exposing to different conditions contiguous stretches of a strip of ventricular muscle of the turtle, Pseudemys concinna, made to beat rhythmically in either direction by artificial stimulation of one or the other end. The details of the method have been described in connection with a search for satisfactory means of depressing conduction in turtle heart muscle (Schmitt, 1928). Various combinations of chambers with partitioning rubber curtains were arranged along the strips. There were always the two end glass chambers and one rubber curtain between them; but in the later experiments the muscle passed through, in addition, one, two or three intermediate hard rubber cells, entailing the use of two, three or four partitioning curtains, respectively. These were used in combination with the various local depressants,

1 The experimental data in this paper are taken from the dissertation presented by Francis O. Schmitt in partial fulfilment of the requirements for the degree of Doctor of Philosophy, Washington University, 1927.
such as electrical polarization, cold and alteration in ionic balance. Resulting from these various treatments of the strip during the course of over fifty experiments, many instances of directional differences in conductivity and of other peculiarities were observed.

In order to facilitate presentation of the relevant data thus accumulated, certain terms will be employed which may be defined here. When the conduction rate through the injured segment of muscle is the same in either direction the state is said to be isodromic; when the rate is faster in one direction than in the other, the condition is said to be heterodromic. A monodromic muscle is one in which the impulse is transmitted in one direction but is blocked in the other; and it is adromic, that is to say, the block is complete, when the impulse can get through in neither direction. Under certain circumstances a second response of one side may follow the response of the other side in the absence of a second artificial stimulation. This return, or reentry, of the impulse is made possible when the muscle is in the opisthodromic state. The corresponding substantives are isodromia, heterodromia, monodromia, etc.

In previous attempts it has been shown (Erlanger, 1906) that mere compression of a strip in a Gaskell clamp may be sufficient to develop directional differences in conduction. In the present experiments each of the rubber curtains exerts some degree of local compression which varied somewhat from preparation to preparation, depending upon the snugness of the fit. The seat of much of the delay in conduction from segment to segment, and of the directional differences in conductivity, was under the rubber curtains and might have resulted merely from the compression they exerted. With the simplest additional treatment, namely, two chambers (one containing a depressant) and one curtain, the impulse, depending upon the direction in which it is moving, passes either from depressed muscle, through a thin disc still more depressed, into normal muscle, or through a sequence the reverse of this. The problem was to produce directional differences in conduction and to determine whether there is any relation between the direction of the heterodromia or monodromia and the sequence of contiguous reactivities. The presence of additional chambers and partitioning curtains probably does not alter the fundamental conditions, but merely increases the chances of eliciting directional differences in conductivity.

It is realized that the method does not accomplish ideally the main end, namely, the division of the strip into contiguous stretches differing sharply from each other in respect to their reactivites. In the first place, as has been stated, the two regions are separated by a disc of tissue whose reactivity is depressed by the compression exerted by the rubber curtain. This compressed region, furthermore, will probably be depressed more by the action of the depressants used than other parts of the strip exposed to them, because, as Clark (1913) has emphasized, the more hypodynamic
the condition of the muscle, the more susceptible it becomes to the action of the reagents. Then, when KCl, for example, is added on one side of the curtain, it penetrates into the muscle of that side and presumably diffuses, though very slowly, into the normal tissue of the other side. This diffusion zone must take the form, roughly, of a cone whose apex protrudes more and more with time into the normal tissue. When the depressant is withdrawn this cone must recede in like manner. The action of the depressant, therefore, is not wholly confined to the side to which it is added. And, finally, it is well known that the response of heart muscle depends to a large extent upon the history of the tissue. In keeping with this it has been found in the present experiments that a second or third treatment with excess KCl, for example, produces effects that are more severe than the first, even when the concentration of the depressant is the same in each trial.

RESULTS. After a ventricular strip has been prepared in the manner previously described (Schmitt, 1928), the readings during the first few minutes usually reveal a slight degree of varying heterodromia; the conduction quotients (i.e., the time in one direction over the time in the other direction) are not constant. This is doubtless occasioned by the residual damage resulting from the manipulation of the strip. As the muscle becomes more normal, the conduction quotients from one period to the next reveal little if any variation from constancy. If, now, one end or the middle segment of the muscle be depressed by pressure, electrical polarization, or by chemical means, the conduction may thereby be much more affected in one direction than in the other, the degree of the difference depending presumably in some way upon the severity of the depression and the reactivity of the muscle.

By way of example, table 1 shows the development of heterodromia following depression by an excess of KCl in an experiment in which four chambers were used. The KCl content of chambers 1 and 2 here was increased temporarily, while the segments in chambers 3 and 5 remained in normal Ringer solution. And table 2 shows the results of an experiment in which the calcium was withdrawn from the Ringer solution of one side. It is seen here that a heterodromic condition rapidly passes over into monodromia during the treatment. The rapidity of the change was doubtless due to the fact that the strip had been previously depressed by an excess of potassium.

Here it may be pointed out that evidences of a fluctuating heterodromia are to be seen in Drury's (1926) experiments, also. This investigator studied the effect of uniformly applied pressure upon conduction in both directions through the auricle of the dog's heart. He concluded that "the general character of the block is identical whether the waves are travelling to or fro through the compressed muscle." Table 3, however, which we
have constructed from his data, reveals that not only does the degree of
decrement vary depending upon the direction the wave is travelling, the
difference being as much as 37 per cent, but also that this heterodromia
fluctuates.

The condition of monodromia has been observed in muscle exposed to
compression alone, and to compression plus either electrical polarization
or chemical action.

### Table 1

<table>
<thead>
<tr>
<th>TIME</th>
<th>1-δ</th>
<th>δ-1</th>
<th>1-δ/δ-1</th>
<th>REMARKS</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:50</td>
<td>0.55</td>
<td>0.53</td>
<td>1.04</td>
<td>Normal Ringer in all chambers</td>
</tr>
<tr>
<td>1:00</td>
<td>0.53</td>
<td>0.53</td>
<td>1.07</td>
<td>Ringer plus 0.07 per cent KCl in 1 and 2</td>
</tr>
<tr>
<td>1:06</td>
<td>0.53</td>
<td>0.58</td>
<td>0.91</td>
<td></td>
</tr>
<tr>
<td>1:12</td>
<td>0.58</td>
<td>0.55</td>
<td>1.06</td>
<td></td>
</tr>
<tr>
<td>1:20</td>
<td>0.62</td>
<td>0.66</td>
<td>0.94</td>
<td></td>
</tr>
<tr>
<td>1:25</td>
<td>0.63</td>
<td>0.68</td>
<td>0.93</td>
<td></td>
</tr>
<tr>
<td>1:30</td>
<td>0.63</td>
<td>0.75</td>
<td>0.84</td>
<td></td>
</tr>
<tr>
<td>1:33</td>
<td>0.63</td>
<td>0.82</td>
<td>0.77</td>
<td></td>
</tr>
<tr>
<td>1:36</td>
<td>0.56</td>
<td>0.85</td>
<td>0.66</td>
<td></td>
</tr>
<tr>
<td>1:43</td>
<td>0.74</td>
<td>0.81</td>
<td>0.91</td>
<td></td>
</tr>
<tr>
<td>1:50</td>
<td>0.80</td>
<td>0.80</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>1:54</td>
<td>0.86</td>
<td>0.87</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>2:01</td>
<td>0.90</td>
<td>0.96</td>
<td>0.94</td>
<td></td>
</tr>
<tr>
<td>2:07</td>
<td>0.85</td>
<td>0.98</td>
<td>0.87</td>
<td></td>
</tr>
<tr>
<td>2:14</td>
<td>0.90</td>
<td>1.06</td>
<td>0.85</td>
<td></td>
</tr>
<tr>
<td>2:19</td>
<td>0.87</td>
<td>1.14</td>
<td>0.76</td>
<td></td>
</tr>
<tr>
<td>2:24</td>
<td>0.91</td>
<td>1.11</td>
<td>0.80</td>
<td></td>
</tr>
<tr>
<td>2:35</td>
<td>0.98</td>
<td>1.09</td>
<td>0.90</td>
<td></td>
</tr>
<tr>
<td>2:42</td>
<td>1.03</td>
<td>1.16</td>
<td>0.89</td>
<td></td>
</tr>
<tr>
<td>2:54</td>
<td>1.29</td>
<td>1.29</td>
<td>0.87</td>
<td></td>
</tr>
<tr>
<td>3:00</td>
<td>1.27</td>
<td>1.48</td>
<td>0.86</td>
<td></td>
</tr>
<tr>
<td>3:05</td>
<td>1.05</td>
<td>1.08</td>
<td>0.93</td>
<td></td>
</tr>
<tr>
<td>3:18</td>
<td>1.69</td>
<td>2.02</td>
<td>0.83</td>
<td></td>
</tr>
<tr>
<td>3:22</td>
<td>1.70</td>
<td>2.21</td>
<td>0.77</td>
<td></td>
</tr>
<tr>
<td>3:30</td>
<td>2.00</td>
<td>1.86</td>
<td>1.08</td>
<td></td>
</tr>
<tr>
<td>3:35</td>
<td>1.93</td>
<td>1.87</td>
<td>1.03</td>
<td></td>
</tr>
</tbody>
</table>

The muscle was contained in four chambers (1, 2, 3 and 6), treadles 1 and 6
recording the contraction of the segments of the muscle in chambers 1 and 6,
respectively.

**Monodromia by compression.** In confirmation of Erlanger (1906) we
have frequently observed in the present experiments during recovery from
complete pressure block a stage during which the block is partial or even
complete in one direction while the sequence is one to one in the other di-
rection. An instance of such unidirectional conduction is seen in figure 1.
In many cases the very first impulse sent through in the better conducting direction may be conducted with the lowest grade of block of the stage of

<table>
<thead>
<tr>
<th>TIME</th>
<th>t-5</th>
<th>δ-1</th>
<th>t-5</th>
<th>δ-1</th>
<th>REMARKS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>seconds</td>
<td>seconds</td>
<td>seconds</td>
<td>seconds</td>
<td></td>
</tr>
<tr>
<td>4:31</td>
<td>0.53</td>
<td>0.72</td>
<td>0.66</td>
<td></td>
<td>Normal Ringer in 1 and 5</td>
</tr>
<tr>
<td>6:23</td>
<td>0.69</td>
<td>0.95</td>
<td>0.70</td>
<td></td>
<td>Ringer minus calcium in 1</td>
</tr>
<tr>
<td>6:57</td>
<td>0.64</td>
<td>0.93</td>
<td>0.66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7:10</td>
<td>0.71</td>
<td>1.17</td>
<td>0.58</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7:13</td>
<td>0.71</td>
<td>1.36</td>
<td>0.45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7:18</td>
<td>0.73</td>
<td>2.01</td>
<td>0.34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7:23</td>
<td>0.74</td>
<td>Block</td>
<td>Block</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7:28</td>
<td>0.77</td>
<td>Block</td>
<td>Block</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7:43</td>
<td>0.81</td>
<td>Block</td>
<td>Block</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7:48</td>
<td>0.80</td>
<td>Block</td>
<td>Block</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The muscle is contained in but the two chambers, 1 and 5.

<table>
<thead>
<tr>
<th>STIMULATING</th>
<th>P-M on M-P</th>
<th>M-D or D-M</th>
<th>P-D on D-P</th>
<th>PER CENT DIFFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>second</td>
<td>second</td>
<td>second</td>
<td></td>
</tr>
<tr>
<td>Proximally</td>
<td>0.0043</td>
<td>0.0073</td>
<td>0.0019</td>
<td>13</td>
</tr>
<tr>
<td>Distally</td>
<td>0.0078</td>
<td>0.0085</td>
<td>0.00163</td>
<td>37</td>
</tr>
<tr>
<td>Proximally</td>
<td>0.0059</td>
<td>0.0075</td>
<td>0.00134</td>
<td>15</td>
</tr>
<tr>
<td>Distally</td>
<td>0.0060</td>
<td>0.0085</td>
<td>0.00154</td>
<td>7</td>
</tr>
<tr>
<td>Proximally</td>
<td>0.0062</td>
<td>0.0098</td>
<td>0.00152</td>
<td></td>
</tr>
<tr>
<td>Distally</td>
<td>0.0068</td>
<td>0.0101</td>
<td>0.00163</td>
<td></td>
</tr>
<tr>
<td>Proximally</td>
<td>0.0061</td>
<td>0.0097</td>
<td>0.00158</td>
<td>-5</td>
</tr>
<tr>
<td>Distally</td>
<td>0.0070</td>
<td>0.0107</td>
<td>0.00177</td>
<td>22</td>
</tr>
</tbody>
</table>

Data in the first three columns are taken from table IV of Drury’s paper. P-D and D-P are conduction intervals between the extreme leads in either direction as indicated (P is the proximal, D, the distal, and M, the middle lead). The differences between P-D and D-P in per cent of the former are given in the last column.

the experiment then obtaining; and a partial one-way block may persist for many minutes. This observation rules out the possibility of explaining the
phenomenon on the basis of a *trepppe* in irritability of the partially blocked side. In the stages pictured in figure 1, conduction was completely blocked for a while in both directions; then a 1–1 sequence developed in one direction without the intervention of any of the intermediate grades of partial block, although conduction in the reverse direction was still completely blocked.

**Impairment following electrical polarization.** A monodromic condition was noted several times developing immediately subsequent to the passage of strong polarizing currents through the strip mounted in the usual manner. Figure 2 shows a record obtained under such conditions near the close of an experiment in which the strip has been exposed to low current strengths; at this time, however, a high voltage (5 volts) was being used. Despite this high potential, and despite the fact that the muscle was being stimulated at a maximal rate, normal conduction persisted. But at the moment the circuit was opened block supervened. This block, however, was unidirectional; it disappeared completely, and perfect sequence returned immediately, when the direction of conduction was reversed, and was complete upon returning to the original direction of stimulation. Figure 2 shows the reversal thrice repeated. The monodromia observed following the application of strong polarizing currents has had no apparent relation to the direction of the polarization. Whether the compression exerted by the curtain is of any significance in determining this effect of polarizing currents, it has been impossible to ascertain.

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**Fig. 1.** Monodromia following pressure impairment. Top line shows contraction of muscle in chamber 6, second line, that in chamber 1; third line signals the stimulating induction shocks; time, on lowest line, is in seconds. The record begins a few minutes after mechanical compression of the muscle, the direction of conduction, as indicated by arrow, a, being from 6 to 1. After three beats the block in this direction becomes complete. a, b, and c show that the block is complete in both directions; d, e, and f show a unidirectionally complete block, the strip beating from 1 to 6 but not from 6 to 1. This record shows that a tendency towards monodromia may develop within 50 seconds after the condition was one of total block.
Fig. 2. Monodromia following polarization by a strong current. Coincident with, and therefore in consequence of, the opening of the polarizing circuit (indicated by rise of upper line) a high grade of partial block in the I-5 direction appears while the sequence remains 1-1 in the δ-I direction. Arrows indicate the direction of conduction. The lowest line signals the induction shocks by which the strip was stimulated, the rate being about 12 per minute. The time line is not reproduced. Greatly reduced.
Impairment by chemical means. Monodromia has been observed in many instances following one-sided chemical action. Table 2, already referred to, shows a case in which a monodromic condition was established following the withdrawal of calcium from the Ringer solution bathing one part of the muscle. The monodromia usually has made its appearance at a time when the conduction rate had been reduced greatly by the depressant; and it would seem that the relation between the reactivities of the muscle on the two sides of the curtain is a factor, as the following experiment indicates. A preparation, contained in four chambers, had been in use for some three hours and conduction had become very slow in both directions. Ringer solution containing 0.07 per cent KCl was then placed in chamber 2. In 15 minutes, the impulse travelling from 2 to 1 was blocked, although conduction was still possible from 1 to 2. In less than one minute, the block in the 2 to 1 direction disappeared, but two minutes later a block in the reverse direction became established; this block from 1 to 2 was permanent. Ten minutes later, segment 2 was again treated with an excess of KCl with the result that in five minutes, the impulse was completely blocked. Thirty minutes after restoring Ringer solution to segment 2 the block in the 2 to 1 direction disappeared, and, under these conditions, a unidirectional block persisted for many minutes. It has been impossible, however, to ascertain whether there is any definite relation between the development of monodromia and the sequence of the reactivities of the parts of the strips.

Heterodromia in relation to the sequence of irritability. Engelmann, in 1895, suggested that the phenomenon of irreciprocal conduction might be due to differences in the reaction characteristics of tissues. If one tissue requires a certain "specific energy" for stimulation and an adjoining tissue less, a unidirectional block may develop, in which the impulse passes from the latter to the former, but not in the reverse direction. Engelmann's quantitative experiments on irreciprocal conduction were done on single fibers of sartorius muscle, and on the basis of them he attempted to account for heterodromia and monodromia in heart muscle. Skramlik (1920) has called attention to a serious difficulty which the Engelmann hypothesis encounters when applied to the conducting system of the whole heart. In the frog heart, in the normal sequence of events, the impulse must pass from the fast conducting auricular fibers through the very slow conducting "block" fibers, into the relatively fast conducting ventricular fibers. If quantitative reaction characteristics play the decisive rôle, then in the normal A-V sequence the impulse must encounter at least one boundary where conditions are very unfavorable for further propagation. Engelmann was very careful, however, to state (p. 281) that irreciprocal conduction must be thought of as being caused not only by quantitative factors of reactivity, but also by qualitative factors, the nature of which is entirely unknown.
In further work upon the nature of irreciprocal conduction, Engelmann (1896) studied conduction in the fibers of large sartorius muscles. The curarized muscles were suspended horizontally with the two ends separated by means of cotton padding soaked in Ringer solution, the muscle being transfixed at the mid-point by pins. Under terminal conditions of fatigue, or following local cooling, he succeeded in producing unidirectional block. In these experiments he sought to localize the effect to single fibers by making incisions into the muscle at the mid-point so that comparatively few fibers conducted the impulse from end to end, and used supramaximal stimuli so as to insure stimulation of all of the fibers still conducting, escape of stimulus across the mid-point being minimized by separating the two ends of the muscle by dielectrics. He was still able to demonstrate monodromia and he consequently concluded that the phenomenon can be exhibited by single fibers, and made the generalization that the impulse is conducted more easily from rapidly conducting tissues to slowly conducting tissues than in the reverse direction. Although his work is now more than thirty years old, we know of no attempts at verification. It might be pointed out that in his experiments, heterodromia was found to precede monodromia even in single fibers (p. 407). This, in the terms of his hypothesis, must mean that in the conduction of the impulse from one hypothetical tissue element to the next, the disparity in specific stimulating energies of the two elements manifests itself in a delay at the junction, provided that each element be considered uniform as regards its conduction properties. This phenomenon of building up of stimulatory energy at junctions at the expense of velocity of conduction is one concerning which little is known, even at this time. It is beyond the scope of this paper to discuss these fundamental questions, but the above considerations suffice to indicate some of the difficulties that confront the Engelmann hypothesis as applied to heterodromia in single fibers.

The experiments in which one side or one segment of the strip is treated with Ringer solution containing four to five times the usual quantity of KCl seemed to afford a means of putting the Engelmann hypothesis to the test. With this in view, the irritability of the muscle in the several chambers was followed by determining the thresholds to electrical stimuli. In 44 trials taken from 14 experiments in which these relative irritabilities were known, 27 indicated that conduction was slowed more when the impulse passed from a tissue of high irritability to one of lower irritability than in the opposite direction, 8 indicated the reverse, while 9 could not be placed in either category. The only conclusion warranted by these results is that there is no constant relation between the irritabilities of contiguous stretches of heart muscle and the conduction rate between them. Indeed, the figures, if anything, contradict the view sponsored by Engelmann, though, as will be made clear below, this is not the inevitable consequence of our results.
The significant result, then, seems to be the lack of any consistency in the direction of blocking relative to the treatment of the strip. A similar lack of consistency is to be noted in other investigations in this field. Engelmann, himself (1894, p. 163), found that sometimes the block in suspended heart preparations was of the A-V type, while at other times it was of the reverse type, although the conditions of the experiments were identical in all cases. Erlanger (1906) found that monodromia occurred under the conditions of his experiments, usually, but not invariably, when the impulse was forced through the strip in one direction over long periods of time. Mines (1914), likewise, noted inconsistencies in results. He says, “in some cases the direction blocked was from the ventricle to auricle, in other cases from auricle to ventricle.” The data of Drury (1925), already referred to, show, upon analysis, a similar variability in the direction of heterodromia when the depression is produced by mechanical compression.

**Discussion.** In view of these inconsistencies in the direction of heterodromia and of monodromia, it seems more reasonable to explain the results of our experiments on a morphological basis. We postulate the existence of multiple conducting pathways in the strip, some conducting better in one direction, some in the other. Upon this basis, heterodromia and monodromia receive a ready explanation if it be assumed that under the influence of depressants and of compression either separately or together, one of these paths is affected later or less than the others and determines the observed conduction characteristics. In all probability the irregular heterodromia observable immediately after the preparation of the strip also is indicative of the existence in the strip of pathways conducting with different degrees of heterodromia, which, owing to the severe treatment it receives, are not the same in the successive contraction cycles. The histology of cardiac tissue, with its multiple branching pathways, is not inconsistent with such an interpretation. Garrey (1914), it may here be recalled, has directed attention to the necessity of assuming local monodromia in ventricular muscle in order to account for the production of circus movements. Skramlik (1920), furthermore, has attempted to explain certain auriculo-ventricular monodromias by means of a similar hypothesis. He found that if all parts of the A-V junction of the frog’s heart be cut with the exception of the narrow dorsal band, or if all parts but this band be cooled, conduction from A to V alone was possible; that, on the other hand, if only the septum be allowed to remain intact, only V-A conduction was possible. He was unable, however, to detect monodromia in the continuity of the ventricular musculature. Skramlik, while admitting in his discussion that his work does not supply the information necessary to ascertain the fundamental nature of monodromia, expresses the opinion that it strengthens the view that conduction in heart muscle may be conditioned by some sort of nervous mechanism. But the present observations, and those
of Erlanger (1906), also, demonstrating that the monodromic condition may develop in ventricular strips, would seem to preclude a neurogenic explanation.

If our results are best explained by assuming pathways in ventricular muscle that conduct better in one direction than in the other, it might follow that they throw relatively little light on the question of the relation of reaction characteristics of contiguous stretches of heart muscle to the transmission of the impulse. For there is always the possibility that the characteristics of the path dominant at the moment so strongly favor a given heterodromia that a chemical treatment calculated to reverse the characteristics of the contiguous stretches that are determining the heterodromia does not suffice to completely overcome the predominant direction of conduction. There is also always the possibility that the particular locus in the path that is determining the one-way conduction may lie at a point that feels relatively slightly the differential action of the treatment to which the two sides of the strip are exposed. To the extent to which this can happen, the method is inadequate as a means of establishing the relation between tissue reactivity and the direction of more ready conduction. Nevertheless, the fact that in over 60 per cent of the cases the delay was greater when propagation was from the more irritable to the less irritable side, if of any significance whatever, is opposed to the view that conduction is facilitated by this particular relationship of tissue characteristics. In any event, it seems fair to assume that there are pathways in the ventricular musculature, which, under normal conditions conduct better in one direction than in the other.

Theoretical. The present experiments throw no light whatever on the fundamental mechanism of heterodromia and monodromia. Engelmann's attempt to account for the phenomena has already been referred to, and nothing further need be said in regard to it other than to repeat that he believed (1896) that they could develop in single fibers. This is equivalent to maintaining in the case of heart muscle, that conduction along the syncytial fibers is not necessarily reciprocal. If so, some device must be hypothesized for the production of this state of affairs other than that which obtains at a nerve synapse, for instance, with its break in direct continuity. Mines (1914) has suggested that "the cause of unidirectional block (at the A-V junction) may very likely be expressed in terms of Adrian's work. If the decrement is uniform, then the system is symmetrical, and the block should be equal in the two directions. But if the decrement is greater in one end of the depressed region than in the other, we may have the possibility that the transmission in the one direction may be easier than in the other." Though doubt has been cast on the existence of decremental conduction in nerve (see for example, Kato, 1926; and Davis, Forbes, Brunswick and Hopkins, 1920), there is, nevertheless, some
evidence indicating the possibility of decremental conduction in heart muscle when injured (Drury, 1926; Schmitt, 1928). Therefore, although the Mines theory is expressed in but the few words quoted, and is based only upon the fact of A-V monodromia, it seems worthy of further develop-

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{fig3}
\caption{Fig. 3}
\end{figure}

...ment. We may imagine that it finds expression in the diagrams \textit{a} and \textit{b} of figure 3. In these illustrative diagrams, segment \textit{B} is a region of depression in which decremental conduction obtains between two untreated, normally conducting segments, \textit{A} and \textit{C}. The lower lines, \textit{XX}, represent the threshold of stimulation to which the tissue will respond, the upper
horizontal lines, the normal impulse strength, and the dotted lines, impulses of subnormal or decrementing strength. Although the impulse in some instances is pictured as dying out in the depressed region, it may be supposed that it might actually reach the junction, but, being subminimal relative to the next segment, be ineffective. Diagram a represents complete block; the decrement is uniform and the system is symmetrical. Diagram b represents a case in which the decrement in one direction is greater than in the other, the condition which, in the opinion of Mines, might make unidirectional block possible.

This conception attributes the monodromia to characteristics of the depressed tissue alone, the reactivity of segments A and C being left out of consideration. It is possible, however, on the basis of decrement, to account for monodromia without assuming that the muscle in the region of the depression has acquired this asymmetrical action on the impulse. Diagrams c and d are constructed on the assumption that the decrement in segment B is the same in both directions so long as the strength of the impulses entering the region is the same. If the strength of the impulse coming from A is less than that coming from C, a unidirectional block might result as shown in diagram c. To this might be added another factor brought out by Schmitt (1928), according to which the actual slope of the gradient would be steeper if the strength of the initial impulse is weakened; this factor would tend to make monodromia even more likely. Again, if the strengths of the impulses from each side are identical but the threshold of segment C raised from the level XX to X'X', monodromia might result as shown in diagram d. This hypothesis seems adequate to account for A-V monodromia without assuming a fundamentally asymmetric decremental state of the fibers of the A-V conducting system.

OPISTHODROMIC ACTION—REENTRY PHENOMENA. In eleven of the later experiments, in which more than three chambers were used, necessitating the use of three or four curtains, a group of phenomena frequently developed which will now be described. The simplest case will be discussed first; it is one in which four chambers (1, 2, 3 and 5) and three curtains were used, the middle curtain, by chance, being the tightest fitting. It will be illustrated by a specific example taken from experiment 40. This experiment had been under way for over four hours. The procedure had been to vary the KCl content of the Ringer solution in chambers 2' and 2, the contents of chambers 3 and 5 remaining normal Ringer solution throughout. Observations relevant to the present topic began at a time when segments 1 and 2 were depressed by KCl. Conduction had fallen to a very slow rate, especially under the curtains, but the depression was not symmetrical; in the 1-5 direction the rate was reduced over 70 per cent more than in the 5-1 direction. Analysis of the partial intervals showed that the point of the greatest delay was at the middle curtain between chambers 2.
and $\delta$ which happened to be the tightest fitting. Here the conduction was exactly 100 per cent faster in the $\delta$-$\iota$ direction than in the $\iota$-$\delta$ direction. At this time an impulse was sent through in the $\iota$-$\delta$ direction, which, after a delay of 2.58 seconds under the middle curtain, elicited successive contractions of the segments in chambers 3 and 5. Immediately a return wave, starting spontaneously, caused a second contraction of segments 3 and 5 in turn. An example of such a return of the stimulus at a later stage of the same experiment is shown in figure 4. The phenomenon developed at a time when the impulse in the $\iota$-$\delta$ direction was rapidly going over into block. Thus when $\iota$ was stimulated a second time, the impulse, as figure 4 shows, was actually blocked, though the speed of conduction in the $\delta$-$\iota$ direction was still fairly high.

In general it may be said that this phenomenon, which is essentially so-called reëntry, makes its appearance at a time when there is a condition of heterodromia bordering very closely upon monodromia; and it usually lasts only a few minutes, though it has occasionally persisted many. The reëntry seemed most likely to develop after one end of the muscle was suddenly and profoundly altered, as, for example, after one side, having been greatly depressed by KCl poisoning, was treated again with normal
Ringer solution, and when, under such circumstances, the direction of conduction was from the poisoned towards the untreated side, though these were by no means the conditions always obtaining.

In seeking an explanation of this phenomenon, two alternative possibilities suggest themselves: the impulse on its round trip either retraces its path or circles back. The former view leads to difficulties insurmountable in the present state of our knowledge; on the other hand, if it be assumed that the impulse travels over different pathways on entering and reentering the depressed region, a simple explanation in accord with the facts can be offered. It will be convenient, in developing this view, to illustrate by the conditions and data drawn from experiment 40 (see fig. 4). Figure 5 is a diagram representing in simplest form the essential conditions of this experiment. A and B are two strata of fibers or two fiber paths passing through a curtain applied at M. Under the curtain, the fibers have been subjected both to pressure injury and to KCl poisoning, and as a result of

![Diagram](https://example.com/diagram.png)

**Fig. 5**

this treatment, the segment between X and Y is the seat of greatly slowed conduction in both directions. Stratum A, being more directly exposed to the compression exerted by the curtain, has been more seriously affected than stratum B with the result that a monodromic condition has been produced in the former. An impulse originating at I and travelling towards X starts, presumably with the same conduction rate, in both A and B. But when the impulse in A arrives at X, it is blocked, owing to the monodromic condition of this section of A, and dies out. The impulse in B, however, traverses the region XY, but at a very slow rate. The pause in this case was 2.50 seconds! Upon leaving the region of depression at Y, the impulse in B spreads out according to the v. Kries (1913) principle of unlimited auxomerie, possibly by means of anastomoses, and goes forward now in both A and B and causes the segments beyond to contract. At the same time, however, the impulse turns back in A, passes through segment YX, which, not having contracted at all, is irritable, and causes segment I to contract a second time. This sequence is made possible first, by the
greater facility with which the impulse enters the region $YX$ from 5 than from 1 as indicated by the conduction times through the strip in either direction, namely, 2.86 seconds from 1 to 5 and 1.43 seconds from 5 to 1. It is made possible also by the sufficiency of the interval of time elapsing between the initial and the final contractions of segment 1, an interval that would include the passage of the impulse through the $XY$ segment both going, which in this particular case is 2.5 seconds, and returning. There are good reasons for maintaining that this time exceeds the refractory period of segment 1. Thus the systolic time, which may be taken as a rough measure of the refractory period, had a duration of 1.5 seconds. And, furthermore, it was observed that a brief exposure of this strip to 0.025 per cent solution of BaCl$_2$ caused a series of contractions with a period of 2.0 seconds, which

must be somewhat longer than the absolute refractory period. To recapitulate then, the conditions that make possible a reentrant beat under the circumstances obtaining in this type of experiment are $a$, monodromic conduction in $A$ in the 5-1 direction, and $b$, a delay in the transmission of the impulse from 1-5 in $B$ sufficient in duration to permit $A$ (and also $B$) in segment 1 to recover from refractoriness.

**Bearing upon ventricular extrasystoles.** This analysis of the conditions determining reentry in strips suggests a simple explanation of spontaneous ventricular extrasystoles of the coupled type in the mammalian heart, based upon the arrangement of the ventricular conduction system. In figure 6, a penultimate twig, $D$, of the A-V bundle is shown dividing into two terminal branches which anastomose with ventricular muscle fibers at $B$ and $C$. 

Fig. 6
Under normal conditions, the impulse from \( D \) reaches \( B \) and \( C \) at approximately the same time, throwing the ventricular musculature at these points into contraction at almost the same instant. But if one of the two terminal branches happened to be the site of a local lesion, or of some other state that depressed conduction in it, the conditions might very well develop which experimentally lead to a reentrant response. It merely would be necessary that the impaired segment between \( A \) and \( B \) become monodromic with conduction impossible in the \( A-V \) direction but still fairly good in the reverse direction. Then an impulse coming from \( D \) would be blocked at \( A \) and would die out, but by way of the other terminal branch it would reach and stimulate the ventricular musculature at \( C \). The excitation from the ventricular fibers would then reenter the Purkinje system at \( B \) and traverse the region of injury, but at so slow a rate that by the time it arrived at \( A \), the uninjured fibers there would have recovered from refractoriness and would again be excited. This excitation would immediately spread through the conducting system and reexcite the entire ventricular musculature. The next normal impulse from the auricle would then supervise to stop this circus movement by rendering the normal fibers refractory. That there could elapse an interval sufficient in duration for the recovery of \( A \) from refractoriness, as required by this hypothesis, is indicated by many published records of greatly prolonged \( A-V \) pauses in man. Barker and Bridgman (1917), for instance, cite cases in which \( A-V \) pauses as long as 0.88 and 1.03 second were recorded.

This conception of the origin of extrasystoles in the mammalian ventricles, it should be pointed out, is not inconsistent with existing electrocardiographic evidence indicating that spontaneous premature beats arise in the conducting system (Lewis, 1925, p. 387). It has the advantage, furthermore, of attributing a phenomenon, which may be almost normal in its incidence, to a lesion, or, it may be, to merely a temporary functional disturbance, in an ultimate and unessential branch of the conducting system. It might be pointed out, though, that a depression or a lesion at any point in the triangular circuit, \( ABC \), of figure 6, or the development in any part of the musculature of a state of affairs comparable to that obtaining in our strip experiments, could cause a reentrant wave by a similar succession of events. As has been said, however, evidence strongly favors the view that the phenomenon in the great majority of the cases develops in the conducting system.

Local circulating rhythms and associated phenomena. A slight modification of the conditions portrayed in figure 5 suffices to supply those needed for the development of a local circus. The impulse returning through \( XY \) from \( 5 \) traverses \( B \) to the left but fails to turn to the right in \( IB \) and traverse \( B \) and \( 5 \) again presumably because the time relations happen to be such that, though \( B \) in segment \( I \) has recovered its irritability, under \( M \) it has not, or because \( B \) at \( M \) conducts the impulse more readily to the
left than to the right and, under the conditions found by the impulse returning from $s$, is monodromic. But if the delay in the return of the impulse were slightly longer, or if the heterodromia were less marked or absent, $B$ under $M$ might also be stimulated by the returning impulse spreading into it from $A1$. Thus would be started a local circus. The part of $B$ in segment $M$ would escape stimulation by the impulse returning in $M$ if (a) the time interval were not long enough for $B$ there to recover its irritability and (b) if the subnormal impulse in $M$ failed to reach the threshold of the relatively refractory $B$ there. Thus the conditions be-

![Image](http://ajplegacy.physiology.org/)

Fig. 7. Multiple response from an extra stimulus. Same conditions as in figure 8. Segment 1 was stimulated as indicated by the arrows. A series of beats follows an extra-systole after the fourth contraction. Two instances of this are shown. Zero points indicated. Reduced.

come clear under which a circus can develop in a comparatively limited locus.

The development of such a local, self-perpetuating circus, together with propagation of the impulse through the length of the strip with each circuit, would account for the responses portrayed in figures 7 and 8. The strip in these experiments passed through five chambers and four curtains. In the case shown as figure 7, four stimuli applied to segment 1 in succession resulted each in the conduction of just one impulse through the strip; but a stimulus thrown into segment 1 so as to produce an extra contraction immediately after the fourth contraction, called forth a long series of regular contractions arising spontaneously in segment 1 and passing thence through the length of the strip.
Stimulation of heart muscle at the end of the refractory period has long been known to induce repeated contractions, circus contractions and fibrillation. On the basis of the observations and views recorded in this paper what happens under such circumstances is that the stimulus is applied to, or passes into some one of the many pathways in the heart musculature that are potentially monodromic. It is obvious that nothing is better calculated to unfold such a monodromia than a second impulse following another early in its relatively refractory period. The possibility is thus provided of the establishment of a circus which may then persist for a

Fig. 8. Multiple response from a single stimulus. The muscle was contained in five chambers, the records being numbered accordingly. A rise in the top line indicates stimulation. Time is in seconds. At the first arrow, segment 6 was stimulated once. This called forth a series of beats without further artificial stimulation. A similar series resulted after a second stimulation, indicated by the second arrow. Reduced.

longer or shorter time. The result would be a tachycardia like that of figure 7.

In essentially the same way it is possible to account for the response pictured in figure 8. Here a single stimulus applied to segment 6 of the quiescent strip produces a series of contractions of the whole strip originating in 6 and causing the other segments to contract in turn. Should a part of the connection between segments 6 and 4 happen to be monodromic either at ordinary rates of stimulation or because of the depressed state that obtains during tissue inactivity, the conditions would be pro-
vided that could lead to the establishment of a circus there. The fact that
the spontaneous contractions cease after a time favors the latter interpre-
tation; they cease because the monodromic state disappears as, with activ-
ity, the reactivity of the strip rises.

Applications to circus movements in the intact heart. In the case of the
intact ventricles a local circus produces the picture of fibrillation because,
on the basis of our views, some of the rapidly recurring impulses arising
from the local circus artificially started, when conducted into the various
pathways in the musculature, are blocked, completely in some, monodromi-
cally in others, and, in the latter event, start other circuses which in turn
act as centers for the distribution of additional rapidly repeated stimuli.
The state of affairs thus produced would be quite like that originally visua-
ized by Garrey (1914).

The excellent accounts of the course of the impulses in auricular flutter
and fibrillation that have come from Lewis' laboratory would lead one to
suppose that potentially monodromic pathways exist likewise in the walls
of the auricles, especially in the vicinity of the mouths of the great veins.
It may be assumed that here the monodromia that permits of the establish-
ment of the local circus develops when the tissue (in the dog) is stimulated
at the rate of about 350 to 500 per minute, and this circus then distributes
impulses at about the same rate producing a tachycardia or flutter of about
that rate in the outlying parts of the auricles. At higher rates of stimula-
tion the potentially monodromic radiating pathways, it may be assumed,
become actually monodromic also, with the result that local circuses
develop in them, and the condition of fibrillation is thus established
throughout the auricular musculature.

Thus, it is seen, the mechanism concerned with the production of coupled
extrasystoles, tachycardia and fibrillation, as has been suggested by others,
may be fundamentally one. Pathways which are potentially or actually
monodromic (and it is to the knowledge of the role of such pathways that
this paper contributes) permit a local circus to develop which produces
extrasystoles or tachycardia and flutter, or multiple circuses to develop
and produce fibrillation.

This, it should be noted, is not Lewis' conception of the inception of the circus.
He holds (p. 320) that at rapid rates of stimulation a wave may find its progress
barred in one direction. The reason for this, he says, is that "the muscle is verging
on the half-rhythm, there are fibres or islets of tissue which fail to respond; and it
may happen that they are at a given instant more concentrated in one limb of the
circle than in the other. In such an instance the wave propagates itself along one
limb only." On such a basis, however, it is difficult to account for the flutter and
fibrillation that result from a single stimulus, and impossible to account for the
monodromia of our strip experiments.
SUMMARY

1. Experimental conditions are described by means of which it often is possible to bring about readier conduction through a ventricular strip in one direction than in the other (heterodromia). When the treatment has been sufficiently severe the condition may go over into one of unidirectional block (monodromia).

2. Monodromia has appeared following depression by local compression, and, in association with compression, by the passage of strong polarizing currents, and by variation in the ionic balance of Ringer solution, locally applied. In the experiments with ionic imbalance there was no rule governing the direction of better conduction; in the majority of trials conduction was faster when the impulse passed from a region of relatively low irritability than when it passed in the opposite direction, though the reverse frequently obtained.

3. This result is interpreted as indicating that there are normally in the strips multiple pathways, some conducting better in one direction, some in the other, the direction of the heterodromia or monodromia being determined by the characteristics of the most resistant or the best protected of the pathways.

4. It is suggested that the Mines theory of auriculo-ventricular monodromia, namely, that the condition may be due to asymmetric decremental conduction in a depressed region, be made more general and modified so as to include strength of impulse and irritability of the responding side as additional variables.

5. In strips passing through multiple chambers and rubber curtains, the phenomenon of re-entry (opisthodromia) has been repeatedly observed. Conduction data presented are consistent with an explanation based on the assumption that a monodromic condition exists in some of the fibers or fiber paths, and a heterodromic condition in adjacent fibers in the region of the muscle under some one of the compressing curtains.

6. Based upon local monodromia in an ultimate branch of the conducting system, an explanation is offered of the mechanism of the coupled type of ventricular extrasystoles.

7. Finally, it is shown how a slight modification of the conditions that produce reentry would lead to the establishment of local circus contractions, and the relation of circus contractions so produced to tachycardia, flutter and fibrillation is discussed.

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