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ON THE INFLUENCES WHICH MODIFY THE WORK OF THE HEART*.

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(*From experiments made in the Physiological Institute of the Berlin University.*)

ONE of the chief objects of these experiments was to study the relations which the auricle and ventricle bear to one another: what part is played by each in their common work of carrying on the circulation. The differences of opinion, which have long existed, as to whether certain of the phenomena of the heart's action are to be ascribed to the one or to the other of its two chief component parts—the auricle and the ventricle—sufficiently indicate how difficult it is to decide such questions from an examination of the mode of action of the entire heart. With the view of avoiding this difficulty, the auricles and the ventricle of the frog, isolated from one another, and from the rest of the animal, were submitted to experimental study, their mode of action being carefully followed under conditions which, while they interfered as little as possible with the vitality of the tissues, were capable of being varied within known limits.

METHODS EMPLOYED.

Of the various instruments which are used for recording the movements of the heart (frog's), there can be little doubt but that the small mercurial manometer, with a floating style for writing on the revolving cylinder, which was first employed by E. Cyon, and which has, since then, been gradually improved in its details by various physiologists, and more especially by Kronecker, is the most accurate. With it the pressure within the ventricle can be regulated at will, while the height to which the column of mercury is raised within the small mano-

* The greater number of the observations here given were contained in a dissertation presented last Spring for the degree of M.D. of Edinburgh University, and for which a gold medal and a half share of the Goodsir Memorial Prize were awarded.

meter tube, the diameter of which is known, gives the measure, not only of the quantity of fluid which the ventricle throws out, but also of the force which it has exerted at each of its contractions. By varying the diameter of the U tube, moreover, the resistance which is offered to the contraction of the ventricle can be varied at will. While this instrument is admirably suited for the purpose for which it was designed, viz., that of recording the rhythm and force of the heart's contractions under varying circumstances, it was not available for the special kind of observations in question. For these latter it was unfitted chiefly because it gives no means of learning with desirable accuracy the changes in the diastolic position of the ventricle, and because we cannot, with it, keep the heart supplied with a constant flow of fresh nutrient fluid, and at the same time, carry on the observation of its movements. The instruments employed by Marey* and by Blasius† bear a superficial resemblance to one used in the experiments recorded in this paper, but neither of them seemed sufficiently accurate for the kind of work required here.

The so-called extra-cardiac method, that by which the movements of the ventricle or auricle are magnified and recorded by means of a lever resting on the heart, need not be noticed further here, as with it there can be no question of anything approaching to an accurate measurement of the force of the contractions.

The instrument which I have used is so constructed as to fulfil the following conditions:—

(*a*) To admit of a continuous flow of nutrient fluid being passed through the cavity of the heart, without interfering with the recording of its movements.

(*b*) To allow of an accurate graduation of the intra-cardiac pressure, which can be kept unchanged at any desired height, from below zero to any point above it which may be wished.

(*c*) To admit of the heart's contracting and relaxing without its thereby causing any change in the intra-cardiac pressure.

(*d*) To record on a moving cylinder the changes in the contents of the ventricle, or auricle, as the case might be, resulting from the contraction or relaxation of their walls.

A glance at Fig. 1, Pl. XV. (two-thirds natural size), where the instrument is represented, will render the description more intelligible.

* Marey, *Travaux du Laboratoire*, 1876 and 1877, and *La Méthode Graphique*.

† Blasius, *Arbeiten a. d. physiolog. Lab. zu Würzburg*, 1872.

The small bell-glass (*a*) rests on a round plate of brass (*b*), to which it is fixed by the aid of a little stiff grease, in the same manner as the bell-jar of an air-pump. In the upper opening of this vessel is fitted a short glass stopper, which is perforated to allow the passage of the heart cannula. This latter is, in principle, the same as Kronecker's* "perfusion-cannula," which I have modified to suit the special requirements of the instrument here in question. It is fixed hermetically in the perforated stopper, and consists of a thin German-silver tube 3 cm. long by 3 mm. in internal diameter, having a series of fine grooves cut at its lower end to keep the ligature, which fastens the auricle or ventricle on it, from slipping downwards. I have found these grooves decidedly preferable to a projecting rim, as they economize space and allow of a larger cannula being used. Inside this cannula is a second tube, of the same metal, measuring about 1 mm. in diameter. It extends from the lower extremity of the cannula to a point about 5 mm. from its upper end, where it passes through its wall, and projects for a sufficient distance to allow of an india-rubber tube being tied on it.

By means of such a cannula, diluted blood, or other fluid, can be kept constantly circulating through the auricle or ventricle which is fastened on it, the rapidity of the flow being regulated by the difference in height of the two reservoirs which are in connection with the larger and smaller of its component tubes respectively.

In the brass plate on which the bell-glass rests are two openings, one being comparatively narrow, and forming the inlet to a short tube which is provided with a stop-cock. This tube (*d*) is intended to permit of the quantity of fluid within the glass vessel being varied at pleasure. The other opening in the brass plate is situated in the centre of this latter, and forms the upper outlet of a short cylinder 1 cm. in length by 1 cm. in internal diameter. Round the outside of this cylinder, at its lower edge, is a groove, to permit of a membrane being fastened on it. The arrangement of this part of the instrument will be readily understood on glancing at Figs. 2 and 3, where it is represented in section.

The membrane used is a delicate, transparent, animal membrane, prepared from the peritoneum of the calf, and often used by perfumers and druggists for fastening elegantly the stoppers of perfume bottles. It is, so far as I can learn, prepared only in Paris, but is readily to be

* Kronecker and Stirling, "Das characteristische Merkmal der Herzmuskelbewegung." Ludwig's *Festgabe*, 1874.

obtained in Great Britain. When moistened with water or glycerine its flexibility leaves nothing to be desired, and its comparative inextensibility specially fits it for the instrument in question. I have found it of great service in the construction of other apparatus for physiological work.

A piece of this membrane is so fastened on the end of the little cylinder of the instrument, that it can move freely up or down. This will be more intelligible on referring to Fig. 3. Through the middle of the membrane (*k*) passes a needle (*e*) which is fixed in the centre of the light aluminium piston (*l*). The lower surface of this piston, which lies on the inner side of the membrane, is fixed to the latter by a little varnish (this is done before the membrane is tied on, while it is still dry), although this is not absolutely necessary, since the valve-like action of the membrane, when the instrument is in use, renders the hole made by the needle air-tight. The diameter of the piston is less by 1·5 mm. than that of the interior of the cylinder in which it is placed, so that it can move freely up and down without friction. It is kept in the centre of the cylinder by means of the guide (*d*) through which the needle passes. The friction is thus reduced to a minimum. The lower end of the needle is connected, by a fine hook (*f*), to the sliding part of a light lever, whose duty it is to magnify, to any desired extent, the movements of the piston. The lever is made of a slip of straw supplied with a delicate aluminium point. The membrane, it should be added, although it be so thin and flexible, is more than strong enough for the purpose required, and, after being once fastened on and moistened with glycerine, will serve for hundreds of observations without requiring renewal.

The ventricle, or auricles, as the case may be, having been fastened on, and the cannula and the reservoirs filled with the diluted blood which is destined to feed the portion of the heart, this latter is introduced into the bell-glass (which has been previously fixed on the plate, and its cavity filled with olive oil), which is closed above by the stopper through which the cannula passes*. On now opening the stop-cock *e* (Fig. 1), the oil begins to flow out through the tube *f*, diminishing

* As the membrane which closes the lower opening of the vessel which contains the heart is permeable to aqueous fluids, it is necessary to use oil with this instrument. This is no disadvantage, seeing that pure olive oil is decidedly preferable to salt solution, which is usually employed to protect the heart, in experiments of this kind, from the action of the air. I have never met with the slightest reason for supposing that oil either stimulates or affects the vitality of the tissue of the heart with which it comes in contact.

the contents of the vessel, and rendering the pressure which exists within it sub-atmospheric, by reason of the suction of the column of oil in the tube.

As soon as the pressure within the bell-glass has fallen sufficiently, the little piston is gradually drawn up. On its having reached the position at which it stands in Fig. 2, Pl. XV., the stop-cock is closed to prevent more oil leaving the vessel. When, now, the heart contracts, it sends its contents out through the cannula, thereby diminishing the quantity of fluid contained in the vessel, which diminution in contents necessarily results in a corresponding rise in the piston, and, with it, of the lever-point. The membrane is arranged so that, with the largest ventricles encountered, the piston can move freely up and down on contraction and expansion without being hindered by the membrane becoming "taut."

The relation which the movements of the point of the lever bears to the quantity of fluid entering or leaving the vessel is most easily learned, for any given position of the sliding coupling of the lever, by direct measurement, *i.e.* by injecting through the cannula (before the heart is fastened on) small quantities (·1 c.cm.) of fluid, and measuring the difference in height of the lever-point after each injection. For this I have generally employed a hypodermic syringe, the accuracy of whose graduation had been carefully tested. By this means we learn also, that the addition, of *e.g.* ·1 c.cm. of fluid, produces an equal extent of movement of the point of the lever whether the latter be inclined downwards or upwards from the horizontal, so long as this inclination is not too great—a limit never reached in the actual observations.

Where it is desired to study, with any degree of accuracy, the influence of changes in the intra-cardiac pressure on the position assumed by the relaxed or contracted heart, it is necessary to fix the zero of the scale, *i.e.* the height at which the reservoir must stand in order to make the pressure within the heart's cavity equal to that of the fluid outside its walls. It is best to find this height by direct experiment, since it necessarily varies with each change in the distance between the sliding part and the fulcrum of the recording lever.

The pressure which distends the wall of the ventricle, when the apparatus is in use, is governed by two factors: (1) the height of the intra-cardiac pressure, which is dependent on the height of the surface of the fluid in the reservoir above the level of the fluid in the cavity of the ventricle; and (2) the height of the extra-cardiac pressure, *i.e.* the pressure of the fluid within the glass vessel but outside the heart wall.

This extra-cardiac pressure is, as has been said, sub-atmospheric, and when we have obtained its exact value, and, counting it as positive pressure, have added it to the pressure which exists within the heart, we obtain the real value of the hydraulic force which distends the ventricle at the given time. When the level of the fluid in the reservoir is higher than that of the fluid in the ventricle, the intra- and extra-cardiac pressures both influence the ventricular wall in the same way, both acting as distending forces; when, on the other hand, the level of the fluid in the reservoir is lower than that of the ventricular contents, these two forces tend to counterbalance one another.

To determine the height at which the reservoir must be placed, in order to counterbalance exactly the extra-ventricular pressure, I have adopted the following method as being both convenient and accurate. A piece of frog's intestine, which has been freed in good part from its lining epithelium by rubbing between the fingers and passing a stream of water through it, is distended with air and dried: when required for use, it is moistened with water and fastened on the cannula, so that a portion, a few millimeters in length, and tied at its free end, represents the auricle or ventricle, its wall, however, playing here a purely passive *rôle*. Being excessively thin and flexible it is well suited for such a purpose. All air bubbles having been driven out of the tubes going to the reservoirs (which are filled with diluted blood), as well as out of the cannula and the little bit of intestine, one of the reservoir tubes is clamped, and the instrument is arranged as if for an actual experiment. On now lowering slowly the one reservoir whose tube remains free, from a point above the level of the fluid in the intestine, we gradually reach a position at which the pressure within the latter has become a little lower than that outside of it, and at which, consequently, it collapses, its collapse being marked by a rise of the point of the lever. With a little care the exact height for the reservoir is sought at which the lever-point takes a nearly medium position between that which it had before and after the collapse of the intestine, and here the zero of the scale is fixed. And when, in the following pages, the intra-cardiac pressure is spoken of, it must be understood that the term is applied, for shortness sake, to represent the true pressure to which the wall of the heart is exposed, as indicated by the height of the surface of the fluid in the reservoir in relation to the *zero* of our scale.

The method which was employed, when it was desired to fasten the ventricle on the cannula, differed in no important point from that used

by Luciani*, Rossbach, and others, and which is practically familiar to most physiologists; it need not, therefore, be again described here. Where the ventricle is very small, the auricular septum may interfere with the introduction of the cannula into the ventricular cavity, and in this case it is most convenient to slit through the septum. This may be very readily done with the help of a pair of very small scissors and a fine grooved director, which Prof. Kronecker has had constructed for the purpose. The director and the pointed blade of the scissors is passed into the ventricle from one auricle while the other blunt-pointed blade enters from the other auricle, and in this way the septum may be slit through without danger of injury to the ventricular wall. A simpler way, but which requires some little dexterity in its performance, is to use a pair of fine blunt-pointed scissors, one blade entering the ventricle from each auricle.

In all the observations on the elasticity of the ventricular wall great care was taken to apply the ligatures as close as possible to the auriculo-ventricular sulcus, always, however, more on its auricular than on its ventricular side. Observations were also made with the ligature fastened round the auricles at various distances from the margin of the ventricle.

The auricle or auricles, as the case might be, were fastened on the cannula in various ways. The most convenient method was found to be the following. The lower two-thirds of the ventricle having been clipped off, the auricular septum is slit through with a pair of fine, blunt-pointed scissors, one blade entering each auricle from the ventricular aspect, great care being of course taken to avoid cutting the walls of the auricles. The *venae cavae superiores* and *inferior* are then ligatured, the position of the ligature round the venous sinus varying in different experiments. The end of the cannula is then introduced into the auricular cavity from the opened ventricle, and is fastened by a ligature running round the sulcus, the upper third of the ventricle, or round the lower part of the auricular wall as the case might be.

In other experiments the *septum auriculorum* was left intact, and only one auricle recorded its movements, the other being closed on all sides. It was attempted again and again, and finally with success, to cut away one auricle completely, so that the septum was exposed, forming the wall of the other auricle whose movements were recorded.

* Luciani, *Berichte ü. d. Verhl. d. k. Sächs. Gesellsch. d. Wissenschaft. zu Leipzig*, 1873, p. 17. Ludwig's *Arbeiten*, 1872, p. 113.

To cut away one auricle, however, without injuring the other, is by no means easy.

On other occasions, again, the cannula was introduced from the venous sinus, the ligature being placed at a varying distance from the margin of the auricle, and the septum being in some cases cut through and in others left intact. It is scarcely necessary to go more fully into the details of these different methods; that which is easiest is the one first mentioned. After a little practice it presents no difficulty and requires very little time in its performance.

A large number of observations were made on the effect of localized stimulation, by means of an induced current, of the different parts of the auricular and ventricular walls. In these cases the following was the method adopted.

The German-silver heart-cannula usually served as the one electrode. The cannula is a little less in diameter than the perforation in the glass stopper through which it passes, and, to make the junction air-tight, the cannula is surrounded by a short piece of thin-walled caoutchouc tubing. Round this india-rubber tube, and separated by it from the cannula, is wound a single layer of tinfoil which is placed in communication with an insulated wire going to one pole of the secondary coil of the induction machine, the other pole of the secondary coil being in connection with the cannula. The roll of tinfoil projects for some distance beyond the inner surface of the glass stopper, and this part is slit up with a pair of scissors into fringes, each about ·75 mm. broad, and long enough to permit of its free end extending further than the furthest part of the auricle or ventricle which is tied on the cannula. These ten or twelve fringes are turned back clear of the heart and of the cannula, one only resting on the heart wall, upon any desired part of which its extremity is made to press lightly. Such an electrode is sufficiently flexible to follow the part of the heart-wall on which its front rests, without the movements of contraction and expansion causing for a moment an interruption of the contact; and its pressure is at the same time so light and equable that there is no danger of injury, even to the exceedingly delicate wall of the auricle. There is no point of the wall of the organ experimented upon which cannot be reached by one or other of the fringes. With electrodes differing so greatly in the extent of surface which is in contact with the heart, the action is necessarily in great part unipolar, and this is by no means the least advantage of the method. The current used was, in all my earlier experiments, from the secondary coil of du Bois Reymond's induction apparatus (medium

size) with one Daniell element in the circuit of the primary coil. More recently I have employed the "influence" apparatus of Tiegel, which is exceedingly convenient in many respects. In these cases the cannula was in connection with the one influence disc, while the tinfoil electrode communicated with the earth by an insulated wire going to the water-supply tube. Two bichromate of potash elements were in the circuit of the primary coil, the medium-sized induction apparatus of du Bois being the one employed, with the secondary completely covering the primary coil. The strength of the current was graduated by varying the distance which separated the two discs of the influence apparatus.

The fluid which was used to supply the auricle or ventricle was composed usually of one part of defibrinated blood mixed with two parts of ·75 per cent. salt solution. The blood was taken either from the rabbit or from the guinea-pig, and was in most instances from the newly killed animal.

During the latter three months of last year I was occupied in investigating the effect produced by various kinds of blood in different degrees of dilution on the action of the frog's ventricle. The full account of the results of these experiments has not yet been published, and it may, therefore, be as well to state shortly here some of the facts learned which bear upon our present subject:

(*a*) The degree of dilution which gave the best results was, for the blood of the rabbit and guinea-pig, that which is given above, *viz.* one part blood to two of salt solution.

(*b*) Serum, whether diluted or undiluted, was found, in many experiments, to be very remarkably inferior in nutritive power to the diluted blood of the same animal.

(*c*) The bloods of the various herbivora (that of the rabbit, guinea-pig, horse, cow, calf, sheep, &c., as well as that of the pigeon) which were examined on this point, were found to have nearly the same nutritive value in each case.

(*d*) Those of the dog, of the cat, and more especially of the pig, while in some instances they were equal in effect to that from the horse or rabbit, were in other examples (from the newly killed animals) apparently almost poisonous.

(*e*) It was also found that, to obtain an equable action of the ventricle, it is necessary that the blood be continuously renewed. Where the contents of the contracting ventricle are changed at intervals, even when these are short, we find that after each "perfusion" the

curve, obtained by connecting with a line the summits of the individual contractions as traced on the cylinder-paper, shews a descending scale, the first few beats being higher than before the fluid was renewed. The renewal of the contents of the ventricle exercises also a very marked influence on the rapidity of the rhythm. In those of the experiments dealt with in this paper, where an absolutely accurate maintenance of a given intra-cardiac pressure was not required, one of the reservoirs was usually placed from one to two centimeters below the other, so that a slow but constant current of fluid was kept up through the ventricular cavity, a great change in the pressure which distended its wall being avoided by using wide vessels for reservoirs with a plenteous supply of the diluted blood, and by removing at short intervals small quantities of fluid from the lower to the upper reservoir. In the experiments recorded in this paper the heart of the water frog (Rana esculenta) was alone employed.

SECTION I.

The Isolated Ventricle.

The ventricle which has been tied on the cannula, by a ligature passing round the auricular wall, near the auriculo-ventricular sulcus, follows, in the most instances, a characteristic rhythm, which has been studied and described with great care by Luciani*. In my own observations the ventricle commenced, in the great majority of cases, by a series of contractions which were at first rapid, afterwards following one another more slowly, and becoming at the same time stronger. This first stage—the *Anfallsstadium* of Luciani—in which the contractions succeed one another with a tolerable regularity, is followed by the "stage of groups" during which a variable number of contractions come together and form a "group," the groups being separated from one another by periods of inactivity of variable duration. Tracing i.†, Pl. XVI., is taken from a ventricle which had entered upon

* Luciani, *l. c.*

† All the tracings accompanying this paper must be read from right to left. In the majority of the tracings the time is not recorded on the abscissa line, the reason being that, owing to the then unfinished condition of the Berlin laboratory, a convenient interruptor did not stand at my disposal. From the excellence of the clockwork, however, which moved the kymograph cylinder, a time-marker was scarcely required, more especially

this stage, and it will serve to illustrate the strikingly characteristic manner in which the contractions follow one another. The groups represented are five in number, the first four being made up each of seven contractions, and the last having eight. In this tracing the curves of the individual contractions are all of the same height, which is due to the fact that the pressure against which the ventricle contracted (25 cm. water) was one against which it was able to empty itself completely at each beat. When, however, the resistance offered to the contracting ventricle is greater than it can fully overcome, *e.g.* with a pressure of 50—60 cm. water, we find that the contractions are not usually equal in force, and in most cases also, the beats forming each group are not separated by equal intervals as is the case in this tracing. Usually the intervals between the beats which make up each group are longer towards its beginning and end than they are in the middle of the group, and in this case the contractions become less powerful at that part where the rapidity is greatest, *i.e.* usually towards the centre of the group. The number of contractions in each group and the length of the periods of inactivity between these, varies greatly in different ventricles and in different conditions as to nutrition, temperature, &c.; as a rule however, in any given ventricle, the number of beats in each group is the same, or nearly the same, as that of those which immediately precede and follow it, while the length of the pauses does not usually differ greatly for the same ventricle at any given part of the grouping stage, so long as the conditions as to nutrition &c. remain uniform. The length of this stage varies greatly with different ventricles and with different circumstances; it may last for from less than a quarter of an hour to two, three hours, or even longer. After the stage of groups, the rhythm of the ventricle passes into the third stage, the "*Stadium der Krise*" of Luciani, in which the contractions follow one another more or less regularly, the rate of beat being however slower than in the first and second stages, and becoming progressively slower while the contractions become at the same time weaker and weaker until they altogether cease. The length of this stage naturally varies greatly, according as the conditions are more or less favourable. In one instance the ventricle

when the cylinder turned with the slow movement which was employed when most of the tracings were taken. By repeated measurements the rate of movement was found almost absolutely equal for a given time, and in the original tracings 38 mm. of the abscissa line corresponds to 1 min. In those tracings which have been reduced this of course changes with the degree of reduction.

was still able to contract thirty-six hours after it had been removed from the animal, and probably many might be kept alive very much longer, if care were taken to renew their contents at sufficiently short intervals of time.

I. The Relaxed Ventricle.

Physiologists seem pretty generally to agree in holding that the ventricle, in the normal condition, expels at each contraction the whole, or very nearly the whole, of its contents. If this be so, and there is every reason to believe in the truth of the generally accepted opinion, it follows that the quantity of blood thrown out at each systole will depend on the degree of distension assumed by the relaxed ventricle. We shall proceed to examine how far the capacity of the relaxed ventricle varies under different conditions.

(a) *Normal Elasticity of the Relaxed Ventricle.*

We have here first to find the extent to which the ventricle dilates during diastole, when the intra-ventricular pressure is varied to a known degree. The instrument which was employed gives the means of varying with accuracy the intra-cardiac pressure, from below 0° to any desired height above 0°, and at the same time enables us to measure the extent of the ventricular dilatation which results, as expressed by the variations in the quantity of blood which the cavity of the ventricle is capable of containing. It may be objected to this method that we cannot from it learn how much the individual muscle fibres of the heart are stretched when its capacity is increased to a given degree, so that we cannot compare absolutely the curve of elasticity obtained in this way with that of a parallel-fibred muscle. Were the ventricle globular, with walls of equal thickness, such a comparison might of course be easily made. It has seemed to me however a matter of much greater practical importance to learn the influence of the intra-cardiac pressure on the capacity of the ventricle during diastole, and thereby on the work done by the heart, as expressed by the product of the quantity of blood thrown out during a given time, or by a given number of contractions, with the height to which it is raised.

The ventricle, when the extra-cardiac pressure is higher than the intra-cardiac, or when these two are equal (at 0° of our scale), while the organ has free play to expand or contract, invariably assumes

a systolic position—its cavity being completely or almost completely obliterated.

In my earlier observations on this subject the reservoir, the height of which regulated the pressure to which the wall of the ventricle was exposed, was moved by the hand up or down a holder on which was fixed a centimeter scale. With this method, errors of one or two millimeters or even more were scarcely to be avoided, and I have lately employed a means whereby the pressure within the ventricle might be governed in a very much more accurate manner. In this latter method the reservoir is raised by the movement of the cylinder upon which the tracings are taken, in such a way that every centimeter of abscissa of the tracing which is obtained corresponds to a rise to the same extent of the intra-ventricular pressure, *i.e.* to a rise of one cm. water pressure. This is readily managed by passing round the upper fourth of the cylinder, which is covered with the blackened paper only on its lower three-fourths, a strong silk thread, forming an endless cord and communicating the movement of the cylinder to a system of pulleys, and by their means raising the reservoir. This latter is counterbalanced by weights, so that, in raising it, the clockwork has only to overcome the slight friction of the pulleys. When used for observation the 0° of the pressure is first marked on the cylinder, the ventricle being replaced by a portion of frog's intestine, as previously described. To mark the 0° the lever-point is placed touching a vertical line which has been previously marked on the drum, while the reservoir is placed at a given level somewhere below what is judged to be the zero of the scale; the position of the lever, with its point at the level of the surface of the fluid in the reservoir, is then carefully marked by means of a needle fixed in a holder. On now setting the clockwork in motion, the reservoir is slowly raised at the same rate as that with which the cylinder-paper passes before the point of the recording lever. On 0° being reached the lever-point falls. This operation is repeated three or four times, the lever-point and the reservoir being carefully placed at the same corresponding positions before the clockwork is set in motion. The tracings thus taken having been found to correspond exactly (as is almost invariably the case), the piece of intestine is replaced by the ventricle. With this latter the same blackened paper is used, and, at the beginning of the tracing, the point of the lever touches the same point on the cylinder-paper, and the reservoir is placed at the same height, as was given to these two respectively before the commencement of the curves, which have already been taken. With the ventricle the pressure reservoir is raised from below 0° to 40—60 cm. above it, and the experiment is repeated 6—8 times, the same blackened paper being used, so that the curves which have been successively obtained lie over one another, and usually correspond exactly when the conditions as to nutrition, temperature, &c., under which the ventricle is placed have been kept nearly uniform. Where these conditions have been changed between the time of taking two individual curves, the changes in the elasticity of the ventricle which result come out with an excessive clearness, scarcely to be obtained by any other method. The normal curve of elasticity of the ventricular muscle is also obtained with a much greater accuracy than would be possible were the reservoir raised and lowered by the hand. We possess also in this method a very perfect means of eliminating any confusion resulting from the "after expansion" (*Nachdehnung* of German writers); for the cylinder can be moved,

and therefore the pressure raised, with the greatest slowness (the rate of movement which I generally employed was one with which the reservoir was raised from 0° to + 50 cm. in about ten minutes). The curve of elasticity obtained by slowly raising the pressure with an equable motion can also, with advantage, be compared with that obtained by slowly diminishing the intracardiac pressure.

The means which may be taken for avoiding the errors to which this method is liable from the escape of small quantities of fluid through the wall of the ventricle will be noticed further on. From the large size of the tracings which are obtained by this autographic method, and the difficulty of reproducing them with absolute accuracy without the aid of photography, it is impossible to give any in illustration of this paper, and I content myself with giving in the chart Fig. iv. Pl. xv. the chief results which can be gathered from one taken from a fairly typical ventricle.

It is only when the pressure within the ventricle is higher than that outside its walls by from ·5 to 1 cm. of water that expansion takes place. The belief, entertained by many of the earlier writers on the physiology of the circulation, that the ventricle possesses the power of active dilatation, has been rejected by most modern physiologists, it being well known that it was founded on faulty observation and experiments. There are, nevertheless, a few well-known writers who still hold fast to the doctrine of an active diastole, among whom may be mentioned Bouillaud, Luciani*, Spring†, Pettigrew‡, &c. More especially in Italy does this view seem to have been gaining ground of late, owing to the unwearied efforts of Luciani in support of his favourite theory§—efforts which have been so successful as to lead to the appearance, from the pen of Mosso and Pagliani‖, of an able criticism defending the more generally received views on the subject. In their experiments these writers employed a method resembling in principle that which was used in the observations which form the basis of this paper. It consisted of an apparatus which admitted of the

* Luciani, *Sulla dottrina dell' attività diastolica*, Bologna, 1874, and *Risposta del Prof. L. Luciani alla critica sperimentàle della attività diastolica*, Bologna, 1876.

† Spring, "Sur les mouvements du cœur et spécialement sur le mécanisme des valvules auriculo-ventriculaires" in *Journal de Méd. de Bruxelles*, 1861.

‡ Pettigrew, *Physiology of the Circulation*, Lond. 1874.

§ Amongst these may be mentioned:—Vincenzo Chirone, "Meccanismo di azione della chinina sul sistèma circulatorio ed azione sulla fibra muscolàre in generàle." *Sperimentàle*, 1874. Guido Tizzoni e Giacinto Fogliato, "Dell' anestesia per le inieziòni intravenòse di cloràlio," *Rivista Clinica di Bologna*, 1875. Socrate Cadet, *Consideraziòni intòrno l' ipotesi di nervi che avrebbero per ufficio d' infrenàre la contrattilità e la tonicità muscolàre*, Roma, 1876.

‖ Mosso e Pagliani, *Critica Sperimentàle della Attività diastòlica del Cuore*, Torino, 1876.

pressures within and without the ventricle wall being made the same, or of the one being made higher or lower than the other, as desired, the organ having at the same time free play to expand or contract. The graphic method was not employed, and the results obtained differ very considerably from those at which I have arrived by oft-repeated experiments. For example, according to Mosso and Pagliani*, the ventricle is able to expand although the pressure outside its walls be higher than the intra-ventricular pressure, so long as the difference in the height of these two pressures does not exceed 1·5—2 cm. (water). It can also be seen from the chart which they give, that, against a resistance of 3 cm. (water), the ventricle was unable to empty itself completely at each contraction, only about $\frac{7}{10}$ths of its contents being thrown out at every systole. How it comes that there are such discrepancies in the results which we have respectively obtained, I do not profess myself able to explain.

If, however, the theory of an active diastole of the ventricle has not recently gained many converts, there is another view according to which also the organ plays more than a passive *rôle* in expanding, and which has gradually been finding more and more favour in the eyes of physiologists. This has moreover the advantage of not requiring the assumption of a new vital property for muscular tissue. I refer to the view according to which the elasticity of the ventricle wall tends to make the latter return after each contraction to a position of equilibrium.

This position of equilibrium is generally assumed to be the same as that which the heart wall takes up immediately after death, and before the post-mortem rigidity has set in. A transverse section through such a heart (the heart of a mammal) shews that the cut surface of the left ventricle describes very nearly a circle, the cavity being by no means obliterated, and it can be seen that, after pressing the ventricular walls together with the hand, they resume their former position with a certain degree of force. This force, in the heart of the freshly killed animal, has been measured by L. Fick† and by Goltz and Gaule‡. The latter observers found that the left ventricle of the calf's heart was able to raise, in expanding, after its walls had been compressed by the hand, a column of water 300 mm. in height, while the aspirating power of the left ventricle of the dog, under

* *L. c.* p. 52.

† Fick, Müller's *Archiv*, 1849.

‡ Goltz and Gaule, "Ueber die Druckverhältnisse im Innern des Herzens," Pflüger's *Archiv*, 1878.

the same circumstances, was represented by a column of from 100 to 200 mm. of water.

Compression by the hand of the dead ventricle has, however, but a very faint resemblance to what takes place when the ventricle empties itself by reason of the contraction of its muscular wall. And for this reason the experiments which have been made by Goltz and Gaule* for the purpose of measuring the minimum and maximum intra-ventricular pressures in the living animal are of very much greater importance. These observers introduced into the left or right ventricle of the dog, by way of the carotid artery or jugular vein as the case might be, a thin-walled german-silver cannula connected with a mercurial manometer by a tube, in the course of which was a valve, opening either towards the heart or towards the manometer, according as the minimum or the maximum ventricular pressure was to be measured. With this apparatus they were able to learn that, with the unopened thorax, the negative pressure in the left ventricle of the dog may be as great as -52 mm. of mercury, as was the case in one experiment; in another it was -36 mm., and in a third it was only -21 mm.; while, for the right ventricle, the negative pressure was in one animal -16 mm. After the thorax had been opened, and the aspirating power due to the elasticity of the pulmonary tissue thus eliminated, they found that the negative pressure within the left ventricle may be as great as -390 mm. water ($= -23{\cdot}5$ mm. mercury), as in one case; in another it was $= -198$, &c. &c.; in one instance the minimum pressure in the right ventricle, under the same conditions, equalled only -10 mm. water. These experiments leave no room for doubt as to the existence of an aspirating power possessed by the ventricle wall and independent of the negative pressure which exists within the thorax generally. This power is evidently, as the authors remark, possessed almost exclusively by the left ventricle, that of the right being practically insignificant. We cannot, unfortunately, learn from these valuable experiments, during how great a part of the diastolic period this suction of the ventricle wall continues, whether it is only for a short instant at its commencement, or whether it continues until the ventricle has nearly reached its full degree of expansion. From a conversation which I have had with Prof. Goltz on the subject I learn that he inclines decidedly towards the former view.

Since the publication of the experiments above referred to, a paper

* *Loc. cit.*

has appeared, from the hands of Prof. Stefani*, in which the author claims that, while the diastolic aspiration is due solely to the elasticity of the heart, as demonstrated by Prof. Goltz, yet this elasticity does not remain constant, that the aspiration may be greater with one diastole than with another, and that independently of the degree to which the ventricle has contracted at the preceding systole. Stefani, however, judged of the variations in the aspirating power, not by the variations in the intra-cardiac pressure, but by the changes in the volume of the entire heart, as indicated by the variations in the pressure of the fluid or air which he introduced into the pericardiac cavity—a method which leaves very much to be desired in the way of accuracy.

I return, after this digression, to the consideration of the influence exercised by the intra-cardiac pressure on the position assumed by the frog's ventricle during diastole. Tracing ii. Pl. XV. and the chart (Fig. iv. Pl. XV.) are intended to illustrate this point. The tracing was obtained by raising and lowering the reservoir, whose height regulated the intra-cardiac pressure, by the hand. It can be seen that at 0° the ventricle was not altogether empty during diastole, being able to send out a small quantity of blood at each contraction. This I am inclined to ascribe to the influence of the cannula, the form of its extremity not being such as to admit of the ventricle wall fitting closely round it. The tracing also shews that, with gradually increasing pressures, the ventricle becomes more and more distended during diastole, but that the increase in capacity does not go *pari passu* with the increase in intra-cardiac pressure. This can be better seen from the chart, taken from a tracing which was obtained by the more accurate method described in the note to p. 464. Taking the intra-cardiac pressures as the abscissæ, and the resulting increase in capacity of the ventricle as ordinates, we obtain a curve of the elasticity of the relaxed ventricle. In the chart this is the lower of the two curves represented, the upper being the elasticity curve of the contracted ventricle. It can be seen that the ventricle is empty at 0°, that with a pressure of 2·5 cm. (water) it contains ·4 cub. cm. of fluid during diastole, at 5 cm. pressure its capacity has increased to ·475 c.cm., at 10 cm. to ·54 c.cm., &c. &c. On raising slowly the intra-cardiac pressure the ventricle begins to distend, therefore, with an internal pressure a little above zero, and above

* Stefani, *Intòrno alle variazìoni del volume del cuore ed alla aspirazìone diastòlica*, Ferrara, 1878.

this, slight variations in pressure produce relatively large changes in capacity until a pressure of 10—15 cm. (water) is reached, above which the distensibility is comparatively small. The elasticity curve of the relaxed ventricle, like that of all tissues of the body (except bone) is a hyperbola, but it differs from that of other tissues, *e.g.* the voluntary muscles, by making a very sharp bend near its commencement, at that part of its course which corresponds to an intra-cardiac pressure varying from 0° to 15 cm.

In order to illustrate the practical importance of the characters of the elasticity or distensibility of the ventricle, which are dealt with above, a portion of what has to be said concerning the contractile power of the auricles may be anticipated here. On fastening one or both auricles on the cannula (the *septum auriculorum* being in the latter case slit through), and measuring the extent to which they are able to contract against different pressures, it is found that, with an intra-auricular pressure as high as 10—15 cm. (water) it is rare that they are able to send out more than a minimal part of their contents (seldom so much as ·01 cub. cm.). Their maximum of work (quantity of fluid thrown out multiplied by the height to which it is raised) is usually obtained with a pressure of from 5 to 7 cm., while the quantity of fluid thrown out is greatest with a pressure which may vary from 2 to 5 cm. Assuming that these values enable us to draw some conclusion as to the contractile power of the auricles in the living normal animal, we may hold that the auricles are incapable of distending the ventricular wall with a force greater than that expressed by from 10 to 15 cm. (water); and that, probably, the normal intra-ventricular pressure during diastole, in so far as it is governed by the force of the auricular contractions, will vary from 2 to 10 cm.

Another element however influences the intra-ventricular pressure during the diastolic period, viz. the height of the blood-tension in the large veins. There is of course no trustworthy method of measuring directly this venous pressure in the living frog. In the course of some experiments undertaken for another purpose I found that, in one case, the *vena cava inferior* burst under a pressure in its interior, of 25 cm. (water). This is, however, of little value for our present subject. More pertinent, though by no means completely satisfactory, seeing that they were made under abnormal conditions, are some direct measurements of the pressure in the small veins which were made by Graham Brown and myself in the course of a series of observations

on the blood-pressure in the capillaries &c.* On submitting a frog, in whose web the capillary pressure was being continuously measured, to Goltz's *Klopf-Versuch*, we found that the blood-pressure in the capillaries gradually falls to 0°. On allowing the animal to recover it was found that the tension in the veins usually begins to rise before that in the arterial system, the result being that the blood commences to flow backwards from the ventricles into the capillaries, and from thence into the arteries. On now measuring the tension in one of the small veins, it was found not infrequently as high as 7—10 cm. (water).

In such experiments the venous system is congested while the arteries are comparatively empty, and when in such cases we find the venous pressure at 10 cm. it may fairly be assumed that it is above that which exists under normal conditions. The normal pressure in the large veins would thus range from 0 to, at the most, 10 cm. The two forces which govern the intra-ventricular pressure during diastole in the healthy animal may then be taken to be only capable of raising that pressure to, at the very most, 15 cm., and, in all probability, the pressure produced by them will usually be under 10 cm. A glance at the chart (Fig. iv.) or the Tracing (ii.) will shew how great is the importance for the work done by the heart of these facts, for, from them we can see, that between the pressures of 1 cm. and 15 cm. the heart expands from a condition in which it is nearly empty to one at which it has nearly attained its greatest possible distension. The conclusion is thus naturally arrived at, that *caeteris* (aortic pressure, rapidity of rhythm) *paribus*, the amount of the heart work is capable of being varied within wide limits by variations in the venous pressure, and more so still by variations in the force of the auricular contractions. In drawing this conclusion we have of course assumed that the quantity of blood entering the heart has been sufficient to give these forces free play, for, unless this be assumed, we must look to the quantity of blood arriving at the heart as the predominating factor in regulating the work done.

The elasticity of ventricles, which have not been too long removed from the animal, and when care has been taken to supply them with fresh nutrient fluid, is remarkably perfect, *i.e.* after distension by a high intra-cardiac pressure it returns, on pressure being reduced, to

* Preliminary notice in *Verhandlungen der physiolog. Gesellsch. zu Berlin*, Sitzung 15th Feb. 1878. Our observations will be published *in extenso* in a succeeding number of this Journal.

almost exactly the same position which it before assumed at the corresponding low pressure. Measurements of this kind are apt to be interfered with by the escape of some of the contents of the ventricle by percolation through its walls†, and, at first sight, it not unfrequently appears that the ventricle, after being distended by a pressure of, let us say, 60 cm., does not return completely, on the tension being lowered to 10 cm., to the same position as it previously occupied at the same intra-ventricular pressure. The amount of fluid which has escaped through the ventricle wall is, however, readily found by lowering the reservoir to a point below the 0° of the scale, when the heart empties itself completely, and the difference in the position of the point of the lever from that which it at first occupied when the ventricle was emptied by the same method, corresponds exactly to the quantity of fluid which has escaped through the thin ventricular wall. This fact is best illustrated when the elasticity curve is obtained by the autographic method, described in the note on p. 464. With this method, curve after curve can be superimposed, and the slightest change in the elasticity of the ventricle is immediately evident in cases where it occurs. I possess several tracings taken in this way, where the intra-cardiac pressure was varied from -5 to $+55$ cm. (water), and where, in each tracing, eight or ten curves are superimposed, each one having been taken so slowly that ten minutes were required to raise the reservoir, with an equable motion, from -5 to $+55$ cm. of the scale. In those cases where the conditions as to nutrition &c. were kept uniform during the course of the experiment, and where, at the beginning of each curve, the slight change in the height of the lever point caused by the escape of fluid through the ventricle wall (where such occurred) was corrected, it can be seen that the individual curves correspond very exactly to one another, so much so that it is usually impossible to tell, from the tracing, how many curves have been taken, often only one somewhat thick line marking the course taken by the point of the lever in the successive tracings. When it is remembered that the delicacy of the instrument is so great that a variation in the elasticity of the ventricle wall result-

* The quantity of fluid which escapes through the ventricular wall, on the pressure being raised, varies greatly with different ventricles. In some, the pressure may be kept as high as 30—40 cm. for as long as half an hour, without any percolation through the wall, while in others this occurs so rapidly that it is impossible, from them, to obtain a reliable elasticity curve. Fig. 2, Pl. XVI., is taken intentionally from a ventricle which permitted unusually free filtration through its wall, the fluid which had escaped collecting in the form of bullæ on its surface. Where the blood used presents traces of commencing decomposition this escape of fluid is usually more marked than with fresh blood.

ing in an increase or a diminution of its contents by less than one hundredth part of a cubic centimeter would be immediately evident on the tracing, it will be understood how perfect is the elasticity of the organ under normal conditions.

When, however, instead of being supplied with diluted blood which is renewed at short intervals, the fluid in the ventricle is left for some time unchanged, or where it is supplied with simple salt solution, its elasticity curve no longer corresponds with that of the normal ventricle. Its elasticity is then usually somewhat less than when it is supplied with plenty of diluted blood, and this is most evident when the rhythm of its contractions is slow; on the other hand, its elasticity not unfrequently becomes greater when the nutrition is insufficient, and this is more especially the case where the rhythm is rapid, and where simple salt solution has been used to replace the diluted blood. Sometimes, under the last mentioned conditions, the elasticity has so increased that the ventricle remains almost completely contracted until the intra-cardiac pressure has risen to 3 or 4 cm. (water). The influence of the rate of beat on the elasticity curve of the relaxed heart, will be noticed more fully further on. Besides the nutrition, there is another influence which modifies the elasticity of the ventricular wall, *viz.* fatigue. Towards the end of the last stage (*Stadium der Krise* of Luciani) the elasticity curve is usually lower on the tracing than it was at first, *i. e.* the ventricle has become more distensible—its elasticity has diminished.

The pathological significance of the fact that imperfect nutrition and fatigue are capable of modifying greatly the elasticity of the ventricular wall, is so evident that it need not be insisted upon here.

It has been said that the ventricle, when the pressures within and without its walls are equal, takes up a position in which it is practically empty. This statement, however, requires to be qualified for certain special conditions. When the curves are taken during the "grouping stage," and when the intra-cardiac pressure is lowered during one of the periods of inactivity which separate the groups from one another, from a position above 0° to one below it, the heart does not usually empty itself completely, but, after contracting until all but perhaps 3 or 4 tenths of the contained fluid has escaped, it remains in this partly contracted condition, even although the extra-ventricular pressure be 6 or 8 cm. higher than that within its walls. It is only when, at the commencement of another group, the ventricle contracts actively that it expels the whole or nearly the whole of its contents. Having contracted, however, it remains so, until forced open by the pressure of the fluid within

its walls. It may be added that the same fact holds good for the ventricle of the tortoise, which, in so far as its elasticity is concerned, resembles very closely that of the frog.

(b) *Modifications in the elasticity of the ventricular wall.*

I. Contraction-remainder. Hermann* appears to have been the first to call attention to a character which not unfrequently presents itself in the curves obtained from voluntary muscles, and which has recently been more closely studied by Tiegel† and others. It is due to the fact that a muscle, whose contractions are being recorded by a myograph, and which is stimulated to contraction by rhythmic excitations—*e.g.* once or twice per second—from an induction machine, frequently does not return, after the first contraction, to the same degree of extension which before existed, but remains somewhat shortened. This shortening of the inactive muscle usually becomes more marked with the first few contractions; afterwards, the muscle being still stimulated rhythmically at the same intervals of time, becoming less and less, until, after a period of time of varying duration, the muscle has very nearly reached the same length as it had before the first contraction. According to Hermann this slow contraction of the inactive muscle is the same in nature as that peculiar slow shortening and expansion which muscles often present under the influence of certain poisons, *e.g.* veratrin, antarin, caffein, &c., and which is sometimes called the idio-muscular contraction. It differs, however, from this latter in so many particulars that it has received a special name, or rather several special names, being called *Contractur* by Tiegel‡, by Hermann§ "contraction-remainder" (*Verkürzungsrückstand*), while Minot‖ styles it "permanent contraction." The name applied to it by Hermann indicates that the shortening results from the foregoing contraction or contractions.

A glance at Tracing iv., Pl. XVI., which is from a ventricle where this "contraction-remainder" is well marked, will suffice to shew in what way it modifies the form of the curve given by the isolated ventricle. From

* Hermann, *De tono ac motu musculorum nonnulla* (Inaug. Diss.). Berolini, 1859. Reference in Canstatt's *Jahresb.*

† Tiegel, "Ueber Muskelcontractur im Gegensatz zu Contraction," Pflüger's *Archiv*, Bd. XIII. 1876.

‡ Tiegel, *l. c.*

§ Hermann, "Notizen zur Muskelphysiologie" in Pflüger's *Archiv*, Bd. XIII. 1876.

‖ Minot, *Journal of Anat. and Physiology*, 1878.

this tracing it can be seen that, after each contraction, the ventricle does not at once expand fully, but that, having at first dilated rapidly, it, when more or less nearly arrived at the degree of distension which existed before the systole, expands more slowly, so that the lever-point traces on the cylinder-mantel a curve whose convexity is turned towards the abscissa. Tracings taken from ventricles during the grouping stage are especially well suited to shew the influence of this factor on the diastolic capacity, as, during the pauses, the ventricle has time to expand, and the difference in height of the diastolic part of the curve before and during the groups, gives us some criterion as to the degree of "contraction-remainder" present at the time of observation.

The degree to which this contraction-remainder influences the capacity of the relaxed heart varies much under different conditions. There is evidence of its presence to a greater or less extent in all those tracings which I possess from the isolated ventricle where the movements of the organ were sufficiently magnified to make slight changes in the form of the curve appreciable. In the case of the ventricle which has not been too long removed from the animal, and which is supplied with good nutrient fluid, the influence of this element on the capacity of the organ is excessively slight, so long as the contractions do not follow one another too rapidly. When, however, the ventricle is supplied with insufficient food, as when, for example, simple salt solution is passed through its cavity instead of diluted blood, it becomes very marked, and the quantity of fluid thrown out at each contraction may on that account be one-sixth to one-eighth less than would be the case were this contraction-remainder absent. It scarcely requires to be added that the influence of this factor on the ventricular capacity varies greatly with the rate of beat. If the interval between the contractions is long, the effect on the quantity of fluid thrown out at each systole may be *nil;* and I may quote, in connection with this subject, the remarks made by Rossbach and Harteneck* on the influence exercised by the rapidity with which the contractions follow one another, on the degree of shortening, in the case of voluntary muscles. They say that "the contraction-remainder only shews itself when the interval between the individual excitations is of a certain duration, and the contractions must follow one another at least once every second. If the interval is longer, there is neither the primary well-marked shortening, nor the later-coming gradual rise of the lever-point above

* Rossbach u. Harteneck, "Muskelversuche an Warmblütern," Pflüger's *Archiv*, Band xv.

the abscissa. If a long interval between the excitations follow a shorter, the point of the lever returns slowly back to the abscissa, and if a short interval succeed a long one which had not produced the contraction, then that now shews itself."

That the "contraction-remainder," or the after-expansion as I would prefer to call it, has not before this been noticed by any of the numerous experimenters who have worked with the frog's ventricle, must be ascribed to the fact that, with the little mercury manometer instrument, it is impossible to follow accurately the changes in the diastolic position of the ventricle. The floating style is far from recording with sufficient accuracy the movements of the mercury upon which it rests to give the form of the individual contractions in a satisfactory manner, even if the inertia of the mercury itself were not a serious barrier in the way of obtaining the true form of the changes in capacity of the organ which occur at each systole.

Before leaving this part of my subject, I may add a word as to the nature of this after-expansion.

Tiegel found it only to occur when the muscle was stimulated directly by the induced current; we learn, however, from the experiments of Rossbach and Harteneck, that it may occur both with direct and indirect stimulation, while, in the case of the ventricle, my own observations shew that it may occur independent of any external stimulation—that it is more or less evident in all ventricle curves, and that it is greatly increased by imperfect nutrition.

It resembles the idio-muscular contraction in some respects, no doubt, but differs from it in one very important particular, viz. in that it is a purely passive phenomenon; and it presents, to my mind, a much closer analogy to a well-known fundamental characteristic of the elasticity of organic substances in general. When a portion of organic tissue—a thread of silk or a piece of artery for example—is stretched by means of a weight fastened to one of its ends, the other being fixed, it does not at once assume the full degree of lengthening which it will ultimately present with that given weight, but, after stretching rapidly to a certain extent, it then expands more and more gradually, until, after a variable time, it reaches a position at which it is really in equilibrium; and when, on the other hand, the weight which stretches it is reduced, the tissue contracts, at first rapidly, and then more and more slowly, towards the position at which its elasticity will exactly counterbalance the weight which tends to expand it. On account of the "after action" (*Nachwirkung*) (which appears to be very slight if not alto-

gether absent in the case of inorganic substances) it is exceedingly difficult to obtain the true curve of various organic tissues. This elastic "after-action" has been studied, and many of its characters indicated, by E. Weber*, who was the first to observe it. It has also received notice from Werthheim†, but it is to Wundt‡ that we are more especially indebted for the chief part of what is known on the subject. The elastic after action is not present to the same extent in all organic tissues, and, in my own observations, I have found it characterize to the highest degree the elasticity of the arterial wall, and of the wall of the veins, while in many other tissues it is relatively unimportant. In muscles, under ordinary circumstances, it is but slight, and the same holds good for the ventricle of the frog. It is different, however, with the ventricle, in that condition where the contraction-remainder is present to a marked degree. When, in this condition, the intra-cardiac pressure is suddenly raised—from 10 to 50 cm. (water) for example—the ventricle takes a much longer time to reach the degree of distension which it finally assumes at that pressure than does the normal ventricle. It is necessary of course, in such experiments, to take the greatest care that no error creeps in due to the escape of fluid through the ventricle wall. If any of the fluid percolate through the wall its quantity may be found by the means mentioned on page 471 and error thereby avoided.

A consideration of the changes in the relations between the elasticity and the distending force, which occur at each systole in the case of the ventricular muscle, will show in what way this elastic "after-action" may influence the form of the curve of each individual contraction, and modify also the diastolic capacity of the ventricle. At the time of contraction the equilibrium between the elasticity of the ventricular muscle and the distending force is broken, not by a change in the degree of force which acts on the walls of the heart, but by a change in the elasticity itself. This view of course does not necessitate the acceptation of Weber's theory that the change in the elasticity is the cause of the contraction. The change, however, in the elasticity, whether it be cause or effect of the contraction, takes place, and, where the elastic "after-action" is present to a high degree, equilibrium between the distending force and the elasticity will not be at once established; and, for the same reason, when, on relaxation occurring, the muscle

* E. Weber, *Poggendorf's Annal.* Band LIV., 1841.

† Werthheim, *Annal. de Chimie et de Phys.*, 3me Série, tome XXI., 1847, p. 385.

‡ Wundt, *Die Lehre von der Muskelbewegung.* Braunschweig, 1858.

resumes the same elasticity which it had previously, the ventricle will not at once assume the full degree of distension which it will ultimately present at the given pressure. This influence of the elastic after action seems to have been entirely overlooked by Fick*, in his experiments on the form of the curve of equilibrium during muscular contraction. Supposing, however, that we accept the view that the contraction-remainder is nothing else than the elasticity "after-action," we are not thereby rendered much wiser, seeing that but little is known as to the intimate nature of this latter.

II. Idio-muscular Contraction. In Tracing iii. Pl. XVI. can be seen the characteristic form of this contraction, caused, in the case of the ventricle from which the tracing was obtained, by the action of digitalis. It can be seen that the ventricle contracts slowly and again slowly expands. In cases where the dose of digitalis has been large, the ventricle remains contracted, and we have the well-known "arrest in systole" of the "digitalis heart." That this slow contraction differs fundamentally from the ordinary systole of the ventricle, is evident from the fact that ordinary contractions are often found superposed upon it, as in the tracing (iii). That it is not tetanus is equally evident. The molecular change, which leads to its appearance, seems to differ in nature also from that which causes the "contraction-remainder," as can be seen from the fact that the ventricle, after each contraction, expands rapidly, and often assumes at once a more dilated position than existed immediately before the systole. This form of contraction in the case of the digitalis heart seems to have more of a toxicological than a therapeutic importance, since, in frogs to which the drug has been administered gradually in small doses, so that death results from chronic poisoning, the ventricle is usually found relaxed. Of the various drugs which cause it, may be mentioned Digitalin, Digitalein, Digitoxin†, Alcohol, Atropin‡, Helleborein, Convallamarin§, Veratrin, Antiarin, Caffein, Rombi poison‖, &c. &c.

It is also met with occasionally independent of the action of drugs, as has been observed by Rossbach¶ in the case of ventricles which

* Fick, "Ueber d. Aenderung der Elasticität des Muskels während der Zuckung." Pflüger's *Archiv*, Bd. IV. 1871.

† Schmiedeberg, *Archiv f. exp. Path. u. Pharm.* Bd. III. 1874.

‡ Luciani, *l. c.*

§ Marmé, *Zeitsch. f. rat. Med.* R. 3. XXVI. and *Göttinger Nachrichten*, 1867.

‖ Fraser, *Proc. of Roy. Soc. of Edin.*, 1869—70.

¶ Rossbach, Ludwig's *Arbeiten*, 1874.

after having been allowed to contract for some time without renewal of their contents, are supplied with fresh diluted blood. I have seen it occur three or four times under these conditions, but it seems probable that, in such cases, its cause is to be sought for in the poisonous action of the products of tissue change which have been accumulating in the ventricle, rather than in the stimulus of the fresh fluid which has been supplied immediately before its appearance. I incline to this view because, when the idio-muscular contraction results from the action of digitalis, it not unfrequently first appears when the poisoned blood is replaced by fresh unpoisoned fluid, as occurred in the case of the ventricle from which the tracing (iii) was taken. Where the dose of the poison is larger, this form of contraction shews itself while the drug is still contained in the cavity of the organ.

Schmiedeberg*, in treating of the intimate nature of the "arrest in systole" of the "digitalis heart," gives it as his opinion that it is caused by a change in the elasticity of the muscular wall which, without diminishing in completeness, has become greater. As to whether the elasticity is as complete as it is normally, is a point very difficult to decide, seeing that the elasticity changes at each part of the curve given by the slowly contracting ventricle wall, and on that account it is not easy to see how the completeness of the elasticity can be accurately measured. The fact noticed by Schmiedeberg himself, *viz.* that, on distending forcibly a heart which has stopped in systole, it may, the distending force having ceased to act, return to its former systolic position only after having contracted and expanded several times, seems clearly enough to indicate that the elasticity during the time of this contraction is anything but complete.

During the time when this idio-muscular contraction is present I have found that the elasticity equivalent of the ventricle wall is in some cases diminished, while in the case of other ventricles, where the proportion of digitalis-infusion contained in the fluid supplied to the organ was larger, it was usually increased. But it must constantly be remembered, in the case of the ventricular muscle, that the conditions under which its elasticity comes into play are by no means the same as they are with the true voluntary muscles. Where the dose of poison has been small, and the idio-muscular curve which is described by the ventricle is not very high, it is usual to find that, on raising the intra-ventricular pressure—*e.g.* from 20 cm. to 30 cm. (water)—the resulting

* Schmiedeberg, "Ueber die Digitalinwirkung am Herzmuskel des Frosches." Ludwig's *Festgabe*, 1874.

increase in capacity of the ventricle is greater than would be the case with the normal ventricle. In such instances, therefore, the elasticity is diminished, as is the case with voluntary muscles in the contracted condition. Where the dose of poison has been relatively larger, and the arrest in systole has occurred, not unfrequently an increase in the distending pressure by 10 cm.—*e.g.* raising it from 20 cm. to 30 cm. (water)—may cause but a very slight increase in the ventricular capacity, much less than would be the case with the uncontracted organ. Here the elasticity is increased. If, however, with a ventricle in this condition, we go on gradually raising the intra-cardiac pressure, we finally arrive at a point where a given increase (10 cm. for example) of the distending force results in a very much greater distension than is given by the relaxed organ under corresponding conditions. The peculiar relations which the elasticity curve of the contracted ventricle bears to that of the inactive organ will be noticed further on, when the influences modifying the force of the ventricular systole come to be considered.

III. Change in Elasticity produced by Goltz's Experiment.—Before leaving this part of my subject, one other condition, in which the elasticity of the heart has become modified, may be shortly noticed. I refer to that condition of the ventricle which is produced by Goltz's* experiment of forcible distension. Tracing v. Pl. XVI. is intended to illustrate the change in the form of the ventricle curve after such sudden temporary raising of the intra-ventricular pressure. This change is always the same in principle, whether the pressure be suddenly raised and again lowered, or whether it be kept raised for some time. It can be seen from the tracing, which was obtained from a ventricle in which the pressure, both before and after the distension, was the same, *viz.* 25 cm. (water), that, after this form of mechanical stimulation, both systole and diastole are less complete, the force of the individual contractions having diminished, and the diastolic capacity being reduced by reason of the slow and imperfect expansion of the organ. In this case the rise in pressure was produced by pinching the indiarubber tube passing from the reservoir to the cannula, and the degree of expansion which resulted can be learned by measuring the extent to which the point of the lever descended. Exactly the same result is produced by suddenly raising and lowering the reservoir. Speaking generally, it may be

* Goltz, Virchow's *Archiv*, Band XXIII. 1868, s. 493.

said that, *caeteris paribus*, the degree to which the ventricular capacity is diminished is in direct proportion to the extent to which the intra-ventricular pressure has been raised, and in inverse proportion to the height of the intra-cardiac pressure which exists after the distension. The rapidity with which the ventricle returns to its previous condition after this experiment seems to depend greatly upon the kind of nutrient fluid supplied to the organ, the rehabilitation being much more rapidly attained with diluted blood than with salt solution alone. A form of curve the same in character, though usually less strongly marked, is often seen at the beginning of tracings obtained from the isolated ventricle, and resulting evidently from the sudden increase in the intra-cardiac pressure during diastole to which the organ is at first subjected. And I believe that the "tetanus" observed by Luciani* and carefully described by him as resulting from the application of a ligature round the auricles, was really caused by the sudden change in the intra-ventricular pressure, which, on connecting the cannula with the other part of the instrument he employed, would necessarily be more or less considerably raised. That form of "tetanus" which he observed on tying a second ligature round the auricles, when the ventricle was already in communication with the manometer, has been shewn by Kronecker† to have been really due to the faulty instrument which was employed.

In none of the tracings which I possess from ventricles which have been submitted to this experiment is there any evidence that this gradual change in the diastolic capacity is caused by an active contraction, as is the case in digitalis heart; it seems to be produced by a purely passive change in the elasticity of the muscle, resembling in some respects that which causes the contraction-remainder. With the ventricle from which Tracing v. was taken the intra-cardiac pressure before and after the distension was relatively high (25 cm.); where, however, the pressure is low, *e.g.* 4—5 cm., the effect of the experiment is that described by Prof. Goltz, *viz.* a "tetanic" contraction of the muscular wall of the organ, lasting for some time. As Kronecker and Stirling‡ have shewn, though it is the nearest approach to true tetanus which occurs in the heart muscle, this condition does not correspond by any means exactly to the tetanus of voluntary muscles.

* Luciani, *l. c.*

† Kronecker, Ludwig's *Festgabe*, 1874, s. 192.

‡ Kronecker and Stirling, *l. c.*

II. Influences regulating the strength of the Ventricular Contraction.

The important results obtained by Bowditch* from his experiments with the heart apex deserve to take a prominent place in treating of this question, and the following quotation from his paper can scarcely be out of place here. He writes, p. 174, "The weakest induction current which causes a contraction of the heart does not produce a correspondingly weak contraction, nor does the force of the latter increase until an insurmountable maximum is reached, when the intensity of the exciting current is raised. With our preparation (the heart apex) an induced current either causes a contraction or it is unable to do so; and in the former case it produces the strongest contraction which an induction current of whatever strength is capable of producing at the given time. From which it necessarily follows that the reason why the contractions of the heart apex vary in force is to be sought for in the variable characteristics of the muscular fibres themselves."

The observations of Bowditch, which have been confirmed and extended by Kronecker and Stirling, relate only to the heart apex; and it is here evidently of importance to learn how far they hold good in the case of the entire ventricle contracting rhythmically under the influence of its own automatic nervous mechanism. The force of each contraction, it need scarcely be said, is calculated, the resistance remaining equal, by the quantity of fluid which the heart throws out. Let us first then seek to learn what is the normal force of the systole when the ventricular muscle is placed under the most favourable possible conditions. The degree of this force, in a fairly typical ventricle, can be learned from the Tracing ii., Pl. XVI., or better still from the chart Fig. iv., Pl. XV., which has already been referred to in connection with the elasticity of the relaxed heart. In the same way as the lower of the two lines on the chart represents the elasticity curve of the inactive heart, so the upper line gives that of the contracted ventricle; or, in other words, the extent to which it has been able to contract against resistances which have been gradually increased.

The first thing which strikes one on examining such a chart is, that the elasticity of the contracted ventricle does not bear the same relation

* Bowditch, "Ueber Reizbarkeit d. Muskelfasern des Herzens." Ludwig's *Arbeiten*, 1872.

to that of the ventricle during diastole, which exists between the elasticity curves of voluntary muscle in the contracted and relaxed conditions. As has been known since the time of E. Weber's investigations on the subject, the elasticity equivalent of the contracted is less than that of the inactive voluntary muscle. From the chart it can be seen that this is only the case with the ventricular wall after the intra-cardiac pressure has reached a given height—a height against which the heart is able and no more to empty itself completely at each contraction, and which it need hardly be added varies with each ventricle, and with the more or less favourable conditions under which it is placed.

In the case of the ventricle from which the chart was taken the heart emptied itself completely against a pressure of from 0° up to 20 cm., and the systole is very nearly complete up to 40 cm., above which pressure the quantity of fluid thrown out at each contraction becomes less and less. The relatively large diameter of the cannula must necessarily place the heart muscle at a great disadvantage in forcing out the last part of its contents, and on that account we are entitled to assume that the systole would be complete in the living animal against a higher pressure than that indicated in the chart; most probably, judging from the form of the curve, the ventricle in question would have been able, had this disadvantage been removed, to empty its cavity completely against an aortic pressure as high as 40 cm.

In this ventricle, then, as in the majority of those which I have examined on this point, the systole is practically complete against a pressure as high as 40 cm.; it is so complete, that the ventricle has lost entirely its red colour at the end of its contraction. In the observations on the blood-pressure in the capillaries &c. of the frog, made by Graham Brown and myself* during the course of last winter, it was found that the maximum tension, *i.e.* the pressure at the summit of the pulse-wave, in the arterioles of the web and tongue of the frog was, in the great majority of the cases in which it was measured (over two hundred), equal to from 25 to 35 cm. (water). That the maximum pressure in the arterioles can be much lower, if any, than the medium aortic pressure is highly improbable. When, therefore, we find that, even after being removed from the animal, the ventricle is able to empty itself completely against a pressure of 40 cm., and in some cases even higher, we obtain some evidence that the ventricle under normal

* Roy and Brown, *Vorläufige Mittheilung in Verhandl. d. physiolog. Gesellsch. zu Berlin*, Feb. 15, 1878.

conditions, in the living animal, empties its cavity at each contraction—a fact which, although it is pretty generally accepted, has been found by no means easy of proof.

Among the influences which modify the force of the heart's contractions, a foremost place is necessarily taken by the nutrition supplied to the ventricular muscle, and its degree of fatigue. The action of these influences has been so carefully investigated by Kronecker*, Merunowicz†, Gaule‡, &c., that there is no need to dwell upon it here, and I have only a word to say on the subject. As is well known, on supplying a ventricle with simple chemically pure salt solution, after it has been contracting for some time with diluted blood, the contractions at once diminish in force. This diminution in force affects the quantity of fluid thrown out at each systole, however, only when the resistance offered to the contraction is not too slight. For example, if, in the case of a ventricle which we have found, by direct experiment, to be able, with diluted blood, to empty its cavity completely at each contraction against a pressure of 35—45 cm. (which I have found a fair average for winter-frogs), we lower the pressure to 15 cm., and then replace the diluted blood with simple salt solution, we do not find, at first, any evident diminution in the force of the ventricular contractions. It is only after a certain time has passed, that the weakening of the systole, which has undoubtedly at once occurred, becomes evident, for it is only when it is contracting against a certain resistance that a diminution of the quantity of fluid thrown out results from a decrease in the force of the contraction. We see thus illustrated the view expressed by Nuël§ (although it follows as a matter of course if Bowditch's observations be accepted as applying to the heart in normal conditions) that the ventricle, in the living animal, probably contracts much more strongly than is necessary to empty its cavity completely.

One element, which plays a part of considerable practical importance in modifying the force of the contractions, is the rapidity of the heart's rhythm, and an examination of the influence of this factor on

* Kronecker, *l. c.*

† Merunowicz, "Ueber d. chemischen Bedingungen f. d. Entstehung des Herzschlages," Ludwig's *Arbeiten*, 1875.

‡ Gaule, "Die Leistungen des entbluteten Froschherzens," *Archiv f. Anat. u. Physiol.*, 1878.

§ Nuël, "Over den Invloed van Vagusprikkeling op de Hartscontracties bij den Kikvorsch," in *Onderzoekingen gedaan in het physiolog. Laborat. der Utrechtsche Hoogeschool*, Derde Reeks II.

the force of the systole, seems best suited to shew how far Bowditch's observations are applicable to the ventricle ligatured above the sulcus.

Bowditch* and Kronecker and Stirling† have shewn, that if, after a long pause of inactivity, the heart-apex be stimulated rhythmically by single induction shocks, its contractions, at first weak, become stronger with each successive beat, in such a way that the curve commences with an ascending scale—the *aufsteigende Treppe* of Bowditch.

This form of curve is also encountered very frequently, after a pause of sufficient length, in the case of the entire ventricle, and the effect of the inactivity, in lessening the force of the contractions, is rendered still more evident when simple salt solution has been used to feed the heart. In the great majority of the tracings which I possess, where an ascending scale of contractions follows a period of inactivity, I find that the contraction-remainder is also exaggerated, and the cause of both of these appears to me to be the same, *viz.* a diminished motility of the muscle plasma—a molecular change which offers a resistance not only to expansion but also to contraction.

As to the question why this resistance disappears gradually with each successive beat, the view brought forward by Kronecker seems best fitted to give a satisfactory answer. The theory which he has enunciated is, that the ascending scale of beats has its cause in the imperfect nutrition which he believes to take place during the pause, and to which the contracting heart is not exposed, seeing that the recurring systoles constantly renew the layer of fluid which is in immediate contact with the ventricular wall.

Whatever be the intimate nature and the cause of it, it is certain that too long a period of rest between the individual beats results in a diminution of their force. On the other hand, too quick a rhythm also results in a weakening of the ventricular contractions,—a fact which is pretty generally recognised, and need not therefore be illustrated by any special tracing. Bowditch has attempted to find the exact length of the interval between the beats which is best suited to give the strongest contractions, and his observations lead him to conclude that these are obtained in the case of the heart apex, supplied with pure serum, when the interval lasts from 4 to 5 secs. My own experiments, which necessarily, from the nature of the circumstances, are not so exact as those of Bowditch, seem to shew that, with the ventricle, con-

* Bowditch, *l. c.* † Kronecker and Stirling, *l. c.*

tracting under the influence of its own automatic nervous mechanism, and supplied with diluted blood, the rate of beat giving the strongest contractions is, with the freshly removed heart, somewhere about 20 per min., which would give a somewhat shorter interval than that found by Bowditch. In the case of fatigued ventricles, or where the nutrition supplied is insufficient, a much longer interval is required to give the maximum contractions of the muscular wall.

The various forms of irregularity, which are so frequently encountered in tracings from the isolated ventricle, have seemed to me to give the best means of testing the influence of the rate of beat on the force of the contractions; and it is from a careful examination of such tracings that I have been led to the conclusions given above. My observations on the entire ventricle confirm fully, therefore, those of Bowditch on the heart apex.

As the relation between the rate of rhythm and the force of the contractions appears to me to have some interest in connection with the clinical diagnosis in cases of irregularity, I may be permitted to make a short digression here. The tracings viii. *a.* and viii. *b.* Pl. XVI. shew each a bigeminal beat, which may be taken as one of the most typical forms of irregularity. These tracings are both from the same ventricle, the one being taken a few minutes after the other, the conditions under which they were obtained being the same in both, with one exception, *viz.*, that in viii. *a.* the pressure against which the heart contracted (15 cm.) was lower than in the case of viii. *b.*, where it was 35 cm. With the low resistance it can be seen that the quantity of blood thrown out on contraction was the same in both of the twin beats, the ventricle having emptied itself completely with each, while with the higher pressure the second beat is considerably less effective than the first. After what has been said above, it need not be insisted upon that, in the case of both tracings the second beat was weaker than the first, and that, if in viii. *a.* the quantity of blood thrown out by each of the twin systoles is equal, it is only because the second contraction, though weaker than the first, was still strong enough to empty the ventricle completely against the comparatively slight resistance opposed to it.

There is, as has already been remarked, no reason for believing that the heart in the living healthy body contracts against an aortic tension which it is just able to overcome and no more; there are, indeed, plenty of reasons for assuming that the power of the heart is, under normal circumstances, considerably greater than is required to

complete its systole. And, in such a case, the occurrence of a bigeminal, or other form of irregular rhythm, need not cause, at the same time, a difference in the quantity of blood thrown out by the individual contractions; since, though some would undoubtedly be weaker than the others, they might still be strong enough, as in the tracing viii. *a.*, to empty the ventricle completely. This is exemplified by the forms of irregularity which result from the presence of certain kinds of "cerebral mischief," in which the aortic pressure is not raised, nor the power of the heart weakened. In sphygmograms from such cases, shewing, *e.g.* the bigeminal rhythm, it can often be seen, that the force of the two beats, as represented at the radial, is the same or nearly the same, indicating that the quantity of blood thrown out by the second of each of the twin beats has not been much, if any, less than that sent out by the first.

It is otherwise, however, in cases of heart disease, where the power of the heart has diminished relatively or absolutely (I refer here chiefly to non-valvular diseases), so that it is no longer greater than is required to empty the heart, and where, indeed, in advanced cases, it is notably less. And when, in such circumstances, irregularity appears—for example, the bigeminal rhythm—the quantity of blood thrown out by each of the twin contractions will differ greatly. As Marey* has shewn, the second beat may be so much weaker than the first, that the intra-ventricular pressure may not be raised enough to open the aortic valves, causing thus intermittence of the pulse, unaccompanied by intermittence of the apex beat.

Assuming that the above views are correct, the conclusion may be drawn—That when, in cases of disease, irregularity of rhythm is present without corresponding irregularity in the force of the contractions, as judged by the height of the sphygmographic tracings, we may take it that the heart's power is greater than is required for it to contract completely with a regular rhythm against the aortic pressure which existed at the time the tracing was taken, and that, therefore, the heart muscle is probably not the seat of disease.

In the foregoing pages it has been sought to shew that, with the entire ventricle, each stimulation from the automatic centre results in as strong a contraction of the ventricle as its muscular wall is capable of performing at the given time. In Tracing vi. Pl. XVI. a form of irregularity may be seen, which might lead to doubts being cast on the gene-

* Marey, *Travaux du Laboratoire*, 1876.

ral applicability of this. This tracing was, however, obtained from a ventricle which had been poisoned by the addition of small quantities of alcohol to the blood which was supplied to it, and the anomalous relation between the rhythm and the force of the beats seems due to a molecular change in the muscle plasma, whereby its elasticity and contractility may be modified by each successive contraction. Where the dose of alcohol is larger, such *bizarre* curves may be obtained as are illustrated by Tracing vii.

III. The Rhythm of the Isolated Ventricle.

When the auricle is ligatured as in Stannius' experiment, and no blood is introduced into the ventricular cavity, the ventricle, as is well known, remains for a longer or shorter period at rest. When, however, the auricles are ligatured round a cannula, through which blood, serum, or other appropriate fluid, is allowed to pass into the cavity of the ventricle, the latter pulsates more or less regularly. The effect of the kind of fluid used is known from the observations of Luciani, Rossbach*, Gaule, &c., and it may be summed up in a few words.

With salt solution, the rhythm during the groups is very slow, and the pauses between the latter long. With serum, the beats come more rapidly, and the groups are separated by shorter intervals; while with diluted blood, the rhythm is still more rapid, and the pauses shorter.

The diluted blood, then, acts as a stimulant, exciting the reflex nervous mechanism of the ventricle.

The question, as to whether the grouping be due to a rhythmic inhibition of the reflex centre, or to rhythmic rise and fall in its excitability, is more difficult; but there are a few facts which seem to point to the latter view. Of these, one is the influence of atropin on the groups, although there is still some doubt as to the truth of the theory of Schmiedeberg, that atropin paralyses the cardiac nerve endings of the vagus. However it be, atropin certainly has not the power of arresting the formation of the groups. I possess many tracings where atropin hearts have given typical groups, even though the drug has seriously

* That Rossbach (*l. c.*) was mistaken in supposing that the serum used by Luciani was the cause of the peculiar rhythm first described by the latter, has been shewn by Luciani himself, *Risposta del Prof. Luciani alla critica sperimentale, &c.*, Bologna, 1876; and in my own experiments the groupings shewed themselves, in almost every case, both where pure defibrinated blood was used and with diluted blood.

weakened the force of the ventricular contractions. Another fact, which speaks against the view that these groups result from a rhythmic inhibition, is, that localized stimulation of the sulcus, by means of weak interrupted currents, never produces slowing or arrest of the beats, but invariably the opposite effect. I have again and again stimulated thus successively every half millimeter of the sulcus, but evidence of the presence of inhibitory nervous elements has never been obtained.

The influence of changes in the intra-ventricular pressure on the rhythm of the ventricle may be briefly alluded to before leaving this subject. The effect of increased aortic pressure, imitated, in the case of the preparation I have used, by closing the tubes connecting the reservoirs to the cannula, so that the ventricle was unable to evacuate its contents, has always been *nil.* The same may be said for most of the cases where the diastolic pressure has been changed, although in two or three cases a sudden increase in rapidity has resulted on raising suddenly the reservoirs which regulate the pressure within the ventricle. Why, in one case, change in the intra-cardiac pressure causes a change in rhythm, and in another not, I have no means of knowing.

SECTION II.

The Isolated Auricles.

In considering the characteristics of the isolated ventricle, the properties of the muscle were first noticed, the elasticity of the latter receiving special attention. In the case of the auricles, however, the difficulties which stand in the way of obtaining anything like exact data as to the elasticity of their walls, are very much greater than with the ventricle. These difficulties arise, not only from the greater delicacy of the auricular wall, and the readiness with which it allows fluid to transude, but they are also due to the fact, that the elasticity of the wall of the auricle is apparently under the direct control of the nervous system. For these reasons it has been impossible for me, as yet, to construct a curve, capable of being applied generally, of the elasticity of the auricular wall, such as has been given for that of the ventricle. Without pretending to anything more than approximate accuracy, it may be said that the auricles are relatively most distensible with an intra-auricular pressure varying from 0° to 3 cm. (water). As to the

perfection of the elasticity, and the extent to which the latter may be modified by the "contraction-remainder," &c., I possess no trustworthy data, and do not, on that account, care to dwell upon the matter here, and the more so that I hope to return to the subject in a future communication, after having studied it more fully with the help of another method of enquiry.

As the chief interest in connection with the action of the auricles seemed to lie in the part played by the nervous mechanism, most of the observations were intended to elucidate that point. The method adopted was that of stimulating locally various parts of the wall of the auricles by the induced current, with the view of exciting the nerve centres which are situated there. The very first experiment, made in this way, shewed that the force of the contractions is capable of being influenced by the nervous system, and that, therefore, Bowditch's law, which was found applicable to the entire ventricle, could not be extended to the auricles as well.

The attempt has been made, by this means of local stimulation, and with a certain measure of success, to find whether evidence could be obtained of a difference in function of the nervous ganglia which are situated in different parts of the wall of the auricles and of the *sinus venosus*.

It is not intended, however, to enter here minutely into this question of localization of function, nor even to attempt to prove that such really exists, and I take this course, partly because my observations on the subject are not yet so complete as is desirable, and partly because the consideration of a question surrounded with so many difficulties would make this paper (already too long) of an unwieldy length. It will only be attempted to shew what the functions are, which these nerve elements are capable of performing, without entering into the question of localization. In all the tracings from the auricles or auricle, which accompany this paper, (Tracings ix. to xxi. Pl. XVII.), the figures on the abscissa relate, not to the height of the intra-cardiac pressure, but to the strength of current employed to stimulate the auricular wall, as already mentioned under the head of the methods used. The mark 0 indicates that the secondary coil was pushed fully up over the primary, and the numbers express the distance of the one from the other, each number being written very carefully at the point where the stimulation began, or where it was changed in strength. The sign – indicates that the electric stimulation was stopped completely at the moment corresponding to the part of the tracing lying immediately above it.

The height of the intra-auricular pressure varied slightly in the different auricles, that pressure being usually chosen at which the largest quantity of fluid was thrown out by each contraction. Whatever the pressure, it was always, in any given auricle, kept at the same height during the time of observation, and the utmost care was taken that a free current of diluted blood should pass continuously through the auricular cavity. These two points are readily attained by using a considerable quantity of diluted blood, so that very wide reservoirs may be employed. In this way, a good deal of fluid may pass from one reservoir to the other, through the heart, without causing any great change in the level of the fluid in the reservoirs. This latter was, moreover, kept as nearly as possible constant, by frequently transferring small quantities of the diluted blood from the lower to the upper vessel. The tracings from the auricles were taken with the same rate of movement of the cylinder as were those illustrating the action of the ventricle, and they must, as well as the ventricular curves, be read from right to left.

I have not thought it necessary to give a tracing of the action of the normal auricle, since several of the tracings which are given shew what is the normal curve at those parts where they have not been under the influence of electric stimulation, or where that stimulation has been very weak. For example, the first parts of Figures ix., x., xiv., xv., xvi., &c., shew the kind of tracing obtained from the isolated auricles where stimulation is not employed. From these it can be seen, that the rhythm is regular, and the force of the contractions equal, and that the rate of beat is much more rapid than is the case with the isolated ventricle. In almost all of the curves represented on Plate XVII. moreover, a certain amount of "contraction-remainder" is evidently present.

Turning to notice the effect of localized stimulation of the auricle wall, Fig. ix. may be referred to, as illustrating one of the results which are most frequently encountered, on passing a weak induced current through a portion of the auricular wall. It can be seen that, when the secondary coil was placed at 8 centimeters distance from the position where it covers the primary coil completely, the auricular contractions became weaker, while the rate of beat remained the same, or very nearly the same. On pushing the secondary coil to 7 cm. distance from the beginning of the scale, the contractions became still weaker, and the interval between the beats was somewhat lengthened. On increasing the strength of the current gradually the same effects became

more and more marked. On ceasing the stimulation at – the contractions quickly became stronger, and the rhythm more rapid.

In Fig. x., which is taken from the same preparation, the place of stimulation only being different, a different effect is found to be produced. In this tracing, it is the force of the contractions alone which is inhibited, the rhythm remaining practically unchanged throughout. On commencing the stimulation, with the secondary coil at 12 cm. distance from the position where the induced current is strongest, it can be seen that the effect on the auricle was *nil;* at 10 cm., the effect was very slight; while on pushing the secondary coil up to 8 cm., a marked weakening in the force of the contractions at once resulted. These latter became immediately afterwards a little more powerful, although the current remained of the same strength. At 7 cm. the same effect was repeated, the weakening being this time more marked. At 6, and at 5 cm., it is still more evident, while on drawing back the secondary coil again to 12 cm. the contractions at once became stronger, and on ceasing the stimulation at – they attained the same height as at the beginning of the tracing.

In Fig. xi., which is taken from only one auricle, a different kind of action is seen. In this tracing stimulation caused a slowing of the rhythm, and an increase in the force of the individual contractions. The same effect can be seen in Fig. xii., which was obtained also from a single auricle.

In Fig. xvi., another result of localized excitation is illustrated. We here find a curious mixture of acceleration and of inhibition—a combination which, it may be added, is by no means rarely met with. Near the beginning of the tracing acceleration of the rhythm and weakening of the beats are at first obtained. This suddenly gives way to slowing of the rhythm, after the secondary coil has stood for a short time at 3 cm. On pushing it up to 2 cm., we obtain a marked acceleration, followed, on the current being stopped, by a short pause, after which the auricles continue to contract in much the same way as at the commencement of the tracing. On again stimulating, at the same part of the auricle wall, and with the sec. coil still at 2 cm., we see, at first, a slow rhythm with weakened contractions result, which passes, however, into an accelerated rhythm, although the conditions to all appearance remained unchanged; and the same result again follows on repeating the experiment, as can be seen towards the end of the tracing. In Fig. xiii. an effect is illustrated, resembling in many respects that shewn in Fig. ix., but differing from it in detail.

In Fig. xiv. again, we have an effect of another kind. Here, acceleration of the rhythm is the chief result of the stimulation. In this tracing it may be observed that, with the sec. coil at 3 cm., an accelerated rhythm alternated with a slower rate of beat; while, at 2 cm., the contractions follow one another so rapidly that the auricles had not time between the individual beats to expand to anything approaching near to their former diastolic position. The same accelerating action is illustrated by Fig. xv.

When certain parts of the auricular wall are stimulated, acceleration alone is produced, while stimulation of other parts invariably results in inhibition, and, after a little experience, one is able to place the electrode so as to obtain, at will, either slowing or quickening of the rhythm. As has, however, been illustrated by the tracings above referred to, slowing or quickening of the rate of beat may occur independently of any change in the force of the contractions, and, *vice versa*, the force of the contractions may be modified without any accompanying change in the rhythm.

It has been remarked, that the elasticity of the auricular wall is apparently under the direct control of the nervous system, and Fig. xvii., xviii., xix., and xx., are intended to illustrate this fact.

In Fig. xvii. can be seen a curious combination of effects resulting from localized stimulation. At first, the rhythm becomes slower and the contractions more feeble, while at the same time the auricle gradually expands. With a stronger current, the contractions become still weaker, while the beats follow one another more rapidly, and the auricular capacity becomes still greater. On ceasing the stimulation, the auricle returns to the same condition as it presented before commencing the excitation. The same result of stimulation is seen towards the end of the tracing.

In Fig. xviii., which is taken also from a single auricle, the same slowing, weakening, and dilatation result from the excitation. I at first supposed, that this change in the capacity of the auricle was due to a local paralysis of the auricular wall at the point stimulated, such as has been described by Schiff, Rossbach, and others, in the case of the ventricle, as resulting from mechanical and other forms of excitation applied locally. Careful examination, however, led me to reject this view, for no change of colour can be seen at the place where the electrode is applied in these cases, and moreover, one not unfrequently obtains curves where this increase in capacity of the auricle is unaccompanied by any weakening of the contractions, such as would neces-

sarily be the case were it due to a local paralysis. Such a curve is represented by Fig. xix., where the change in the capacity is unaccompanied by a change, either of rhythm, or of the force of the contractions. It should be mentioned, that this change in capacity, which not infrequently results from stimulation of certain parts of the auricular wall, is very much influenced by the nutrition supplied to the organ. Where this is good in quality, and where a free current is kept up through the auricular cavity, the auricle expands much more readily on the stimulation being commenced, and resumes its former capacity much more rapidly on the stimulation being brought to an end.

Fig. xx. is given as an illustration of another of the numberless combinations of effects which result from localized excitation. Here, at different parts of the tracing, can be seen both slowing and acceleration of the rhythm, inhibition of the force of the contractions, and increase in capacity of the relaxed auricle.

These tracings will suffice to shew how different are the properties of the isolated auricles from those of the ventricle. As has been said, I have seen reason for believing, from these observations, that the different groups of nerve-cells, situated at various parts of the walls of the *sinus venosus*, auricles, and auricular septum, are endowed with different functions, and I hope soon to be able to treat of this subject more fully. The actions of these different centres combine, in normal circumstances, to give a regular rhythm to the heart's contractions. I have made a few observations on the relative irritability of two centres having antagonistic properties, and have found that seemingly the accelerating or reflex centres are the most powerful, *i.e.* their action usually predominated when both an accelerating and an inhibiting part of the auricle wall were stimulated at the same time with the same strength of current. There are, however, so many possible causes of error present in experiments of this kind, that the greatest caution must be exercised in drawing conclusions from them.

One effect, however, of stimulating two parts of the auricular wall at the same time may be referred to, *viz.* the not infrequent appearance of various forms of irregularity.

An example of this is seen in Fig. xxi., which was obtained from the isolated auricles of a frog which were stimulated at two points,—one, near the margin of the *sinus venosus*, on the posterior aspect of the heart, close to the insertion of the *septum auriculorum*, and the other, at the auriculo-ventricular sulcus, near the aortic bulb (Munks' ganglion). The tracing shews groups, each formed of three beats, and

arranged together in such a way as to produce secondary groups also made up of threes, constituting thus a complex form of irregularity of rhythm. In a paper published by me in the *Edinburgh Medical Journal* for this year (Jan. number), it will be found stated, that certain regular forms of irregularity of the heart may, very probably, be due to an "interference" of the action of the accelerating and inhibiting nervous elements, which are situated in the walls of the organ. The Tracing xxi., as well as many others which I have obtained by the same means, afford some considerable support in favour of such a view.

Conclusion.

The valuable observations made by Nuël*, under the guidance of Prof. Donders, on the influence which is produced by stimulation of the vagus on the action of the frog's heart, do not, as yet, seem to have attracted the attention to which they are entitled from their important bearing on the physiology of the heart. Nuël seems to have been the first to demonstrate that the weakening of the systole, which results from vagus excitation, affects only the auricle—a fact which he shewed to be applicable in the case of the mammalian heart, as well as in that of the frog. He also shewed that the weakening of the systole does not go hand in hand with the slowing of the rhythm, which likewise results from excitation of the vagus; that these two phenomena present no parallelism, and are presumably dependent on the action of different nerve elements. He thus confirmed and extended the observations of Bowditch, Kronecker, and others, which had been made on the heart apex. It is believed that the experiments recorded in the foregoing pages enable us to advance still further in the same direction. I do not intend to give here a *resumé* of the matter contained in the body of this paper, and only wish to indicate briefly how my observations enable us to answer the question stated on the first page of this communication, *viz.*—"What are the relations which the auricle and ventricle bear to one another—what part is played by each—in their common work of carrying on the circulation?"

It has been shewn, in the foregoing pages, that the height of the intra-cardiac pressure during diastole plays a predominating part in

* Nuël, "Over den invloed van vagusprikkeling," &c. in the *Onderzoekingen ged. in het physiolog. laborat. d. Utrechtsche Hoogeschool*, Derde Reeks II. 1873.

regulating the capacity of the ventricle, the elasticity of whose wall is of such a nature, that the organ is most distensible with forces of such a strength as are capable, in the living animal, of being brought to bear upon it. As each contraction of the ventricle, in normal circumstances, empties its cavity completely or almost completely, the quantity of blood thrown out depends upon the degree of distension during diastole. And, since the amount of the force which distends the ventricle is in great measure dependent on the strength of the auricular contraction, it follows that, *caeteris paribus*, the work of the heart, in the living animal, is governed chiefly by the auricle, the ventricle influencing the amount of work done only indirectly.

The elasticity of the ventricular wall has been shewn to be remarkably perfect, but that, under the influence of various causes, this elasticity may become modified in different ways, which have, however, the common result, that they tend to interfere with the perfect performance of the function of the heart. It has also been pointed out, that the elasticity of the ventricular muscle, and the modifications to which it is liable, are of the highest importance, not only from a physiological, but also from a pathological point of view.

The nervous elements situated in the walls of the auricles and venous sinus are destined to regulate the work of the heart, but they act in an altogether different manner on the auricle and on the ventricle. For the ventricle, they have only the power of regulating the rapidity with which the contractions follow one another, while they are capable of influencing the movements of the auricle in a very considerable variety of ways.

We have seen that localized stimulation may produce, as a primary result, not only weakening, but also increase in the force of the contractions, that it may cause not only slowing, but also increased rapidity of rhythm, and that it may produce active dilatation of the relaxed auricular wall, by modifying directly the elasticity of the latter. I do not doubt that it will sooner or later be demonstrated, that diminution in the capacity of the relaxed auricle may also result primarily from stimulation. These different effects, which are produced by localized excitation of the auricle wall and of that of the *sinus venosus*, appear in a manner which shews that they are more or less independent of one another, and, on that account, we are justified in believing them to be due to the action of specifically different nerve elements. But besides this, as has been stated in the body of this paper, although, for various reasons, the fact has not been insisted upon, my observations have led

me to conclude that these elements are not only distinct in function, but that they are also differentiated as to locality.

It is through its influence on the auricle, which must be looked upon as a much more highly developed organ than the ventricle, that the nervous system regulates the work done by the heart.

In conclusion, I must record the debt of gratitude which I owe to Prof. Kronecker for the kind assistance which he has given me in making these observations. Not only has he afforded me much valued advice, but he also stood by me with unwearied activity in overcoming the difficulties which lay in the way of making the experiments—difficulties which principally arose from the then unfinished condition of the New Berlin Institute.

STRASSBURG,
Oct. 1878.

Fig. 1.

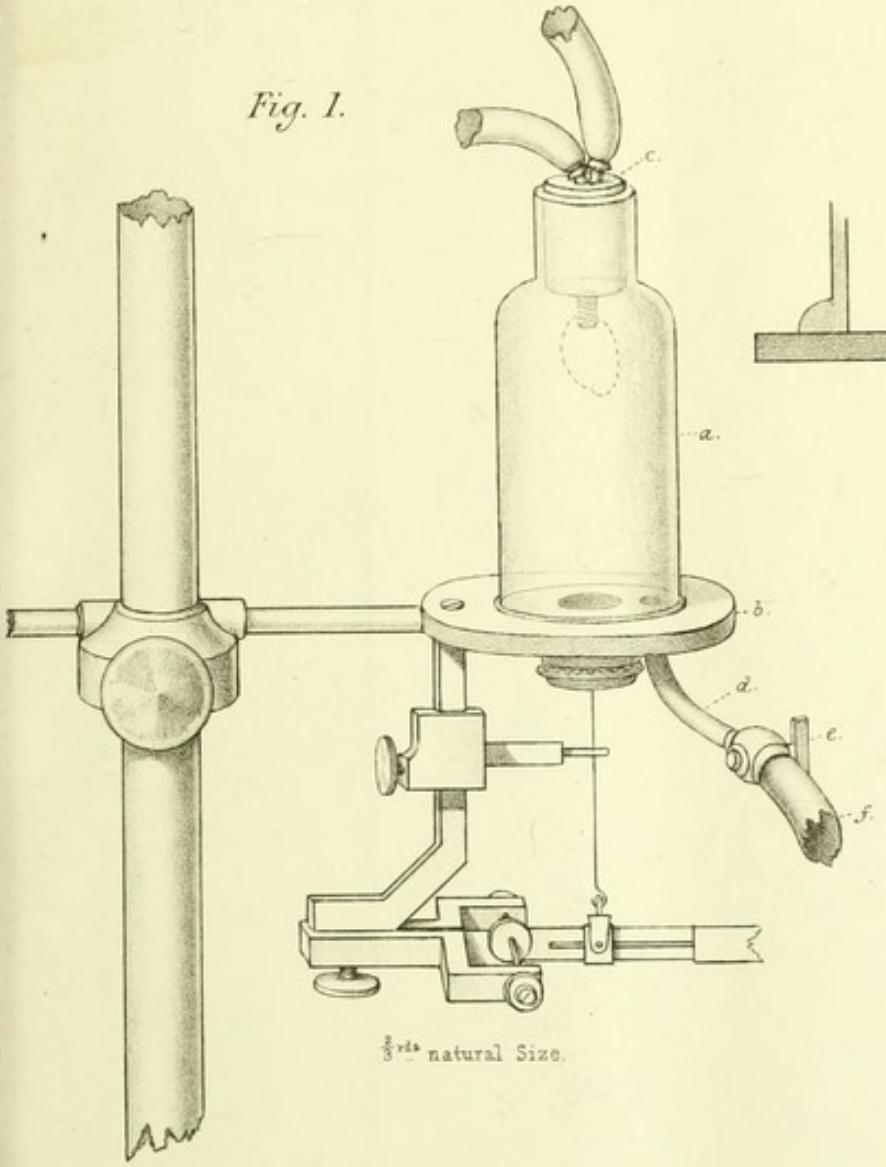

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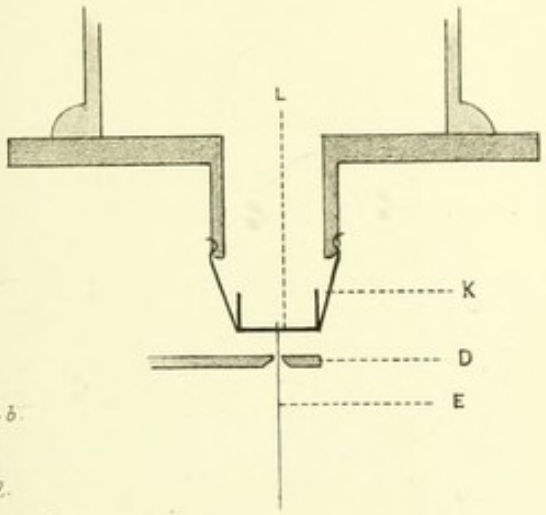
Fig. 3.



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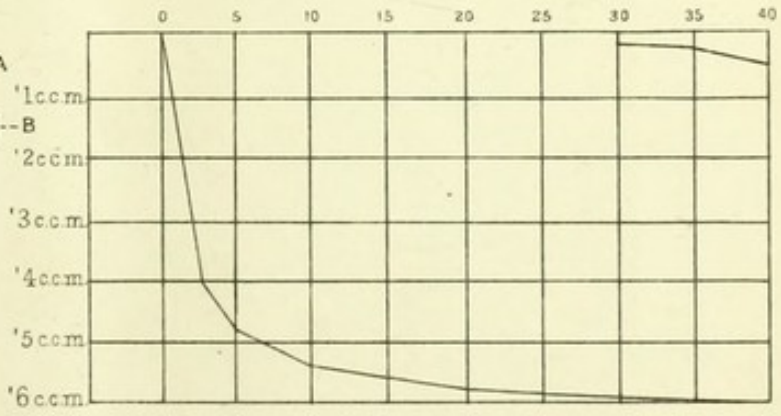

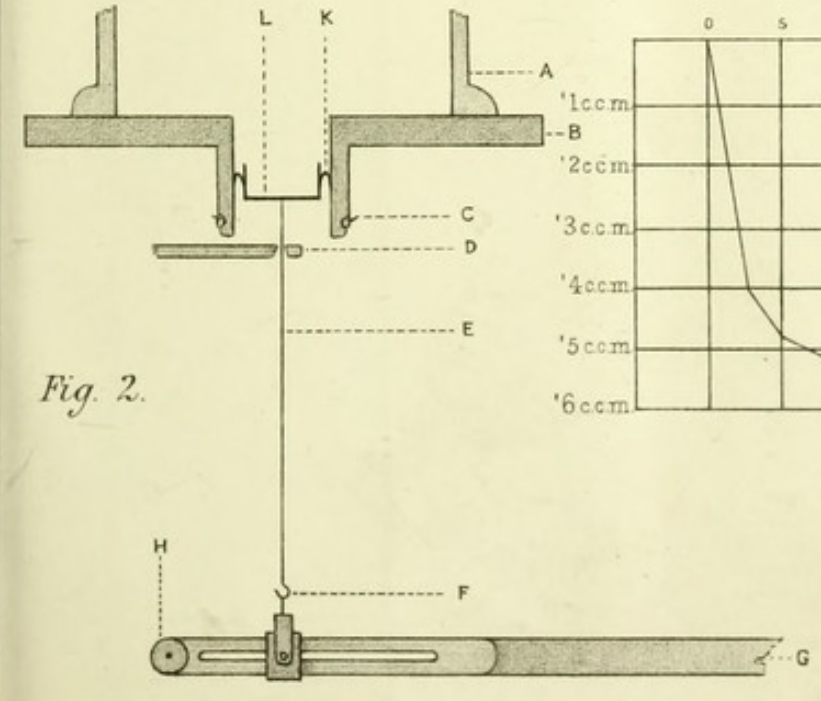

Fig. 2.

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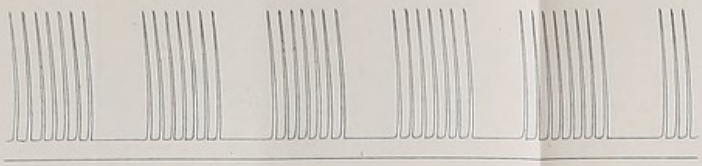
Fig. 1.



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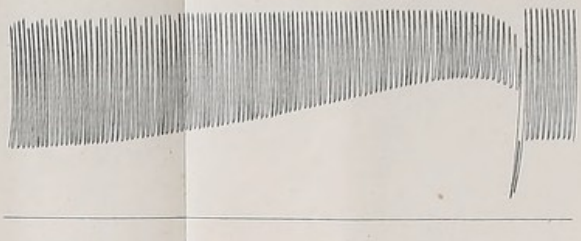
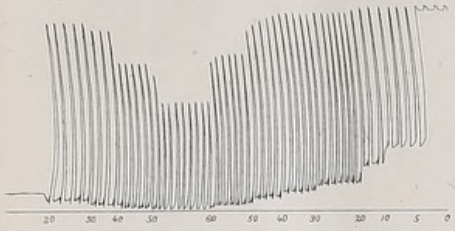


Fig. 2.



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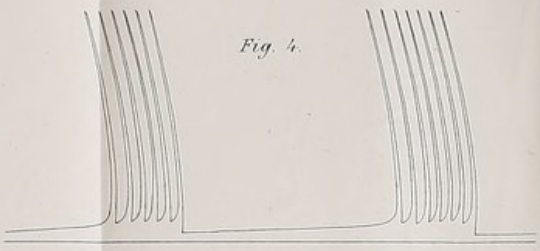
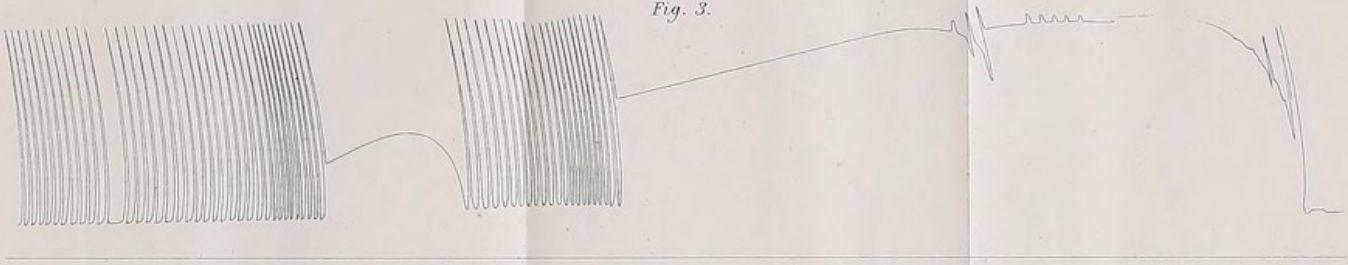


Fig. 6.

Fig. 3.



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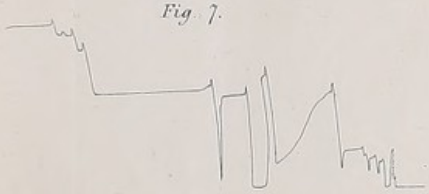

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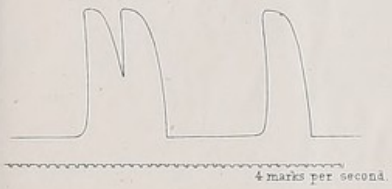

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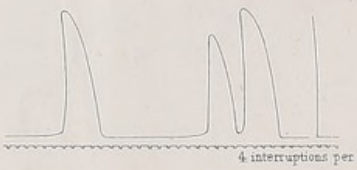

The tracings represented on this plate are reduced to one half of their original size.

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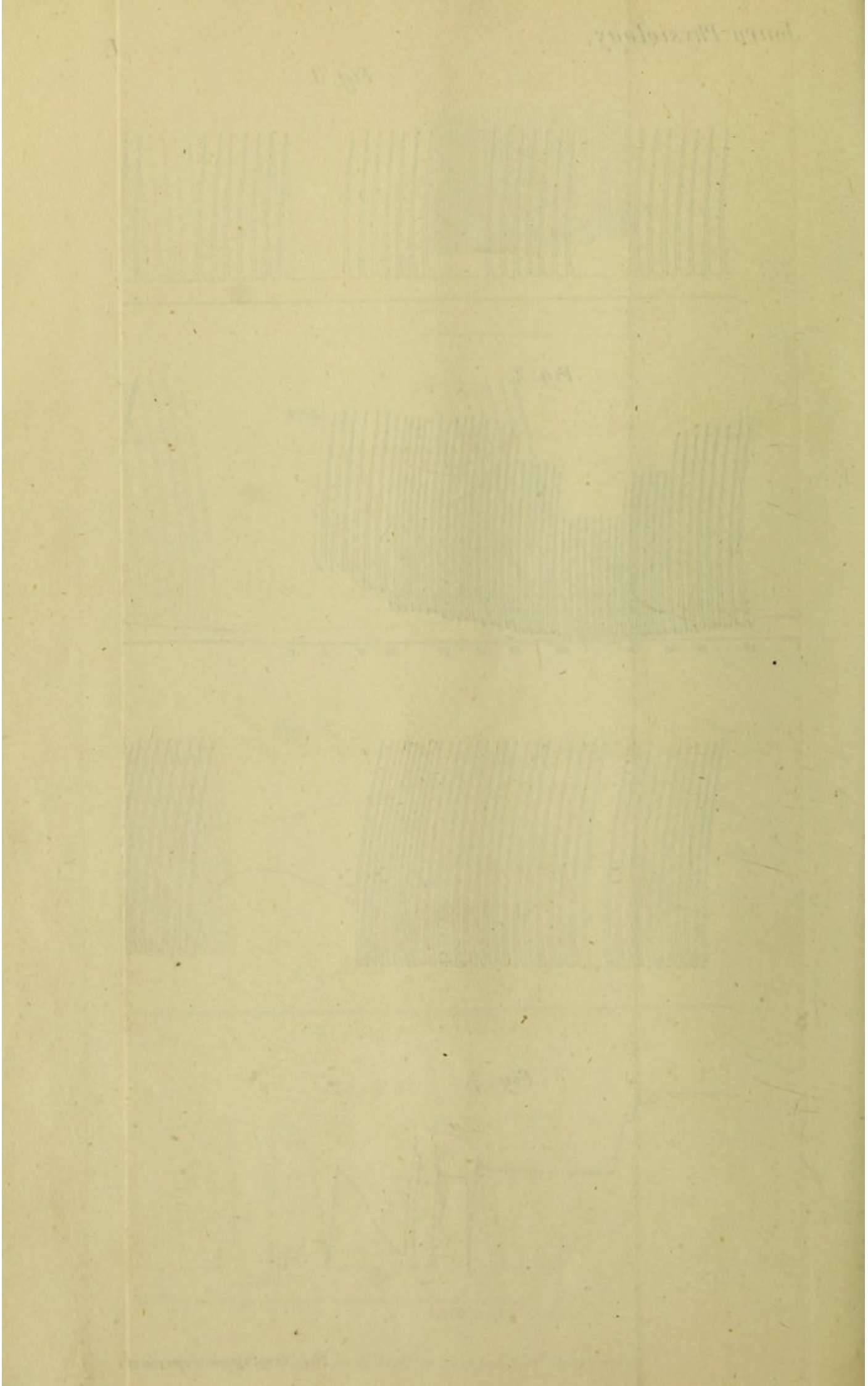

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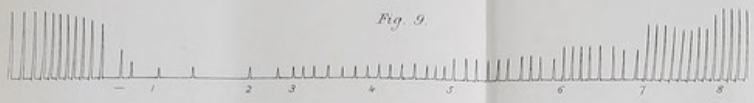

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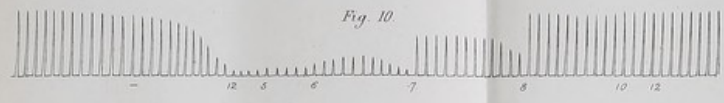

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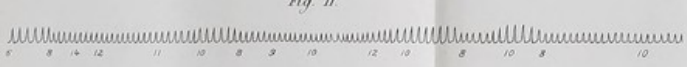

Fig. 12.

Fig. 16.

Fig. 13.

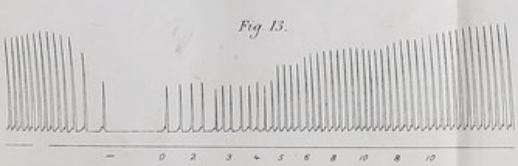

Fig. 14.

Fig. 15.

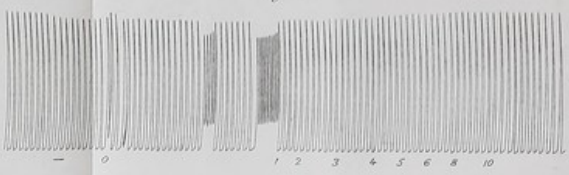

Fig. 17.

Fig. 18.

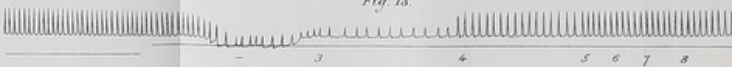

Fig. 19.

Fig. 20.

Fig. 21.