

Physiology. — “*On the Alpha-automaticity of the Autonomous Organs.*” By Prof. H. ZWAARDEMAKER.

(Communicated at the meeting of June 24, 1922).

In the organism there are some organs which perform automatic movements and whose movements are continued also in parts that have been isolated from the body. Without any outward stimulation, simply by watching those parts we can follow up the continuation of this action in its causal and conditional relations. The type of such an organ is the heart. It is the musclecells themselves that pulsate, from the earliest embryonal existence up to death. Such a pulsating heart-cell is comparatively a simple system of phases,¹⁾ which, if the nucleus is left out of consideration, is made up of the following components: 1st. 7 ions, H, OH, Na, K, Ca, HCO₃, H₂PO₄ (resp. HPO₄); 2nd. 2 lipoids, cholesterin and lecithin; 3rd. a carbohydrate, glycogen, which is alternately combined with phosphoric acid and isolated from it again; 4th. oxygen; 5th. proteins and water as a solvent. The absolute quantity of every component exerts, according to the rules of the equilibrium of the phases, an influence upon the whole. Influence may be exerted, a component may even be given a certain concentration, by surrounding the cell with a nutrient liquid composed for the purpose. In so doing substitution appeared to be possible. Na may be replaced by Li or by highly purified Cs; K by all radio-active elements²⁾; Ca by Sr and Ba; lecithin by sodiumoleonate. Besides the absolute quantity also the mutual relations carry weight, notably H : OH, H : HCO₃, K : Ca. Such interrelations must keep within certain bounds. To test this various qualities of the function may be considered: first of all the so-called tonus-condition, i.e. the degree of continued contraction between the limits of atony and maximal tonus; next the excitability in the several intervals of a period; lastly the automatic movement itself. Now granting the conditions of the system to be so regulated that the bounds we alluded to, have been kept in view, and each

¹⁾ H. ZWAARDEMAKER, *Erg. des Physiol.* Bd. 5. p. 135. 1906.

²⁾ H. ZWAARDEMAKER, *These Proceedings* Vol. XIX, p. 633. (1916).

of the three fundamental manifestations, i.e. tonus, excitability and automaticity persist freely, two sorts of automaticity can be elicited by superadding successively the several radioactive elements to the nutrient liquid which surrounds the cells. Two sorts we say, because there are two groups of radio-active elements, which thus far I have been able to use as medium in the solutions of RINGER or TYRODE to substitute vice versa: 1st. an α -group: uranium, radium, emanation, polonium, thorium, 2nd a β -group: potassium, rubidium.

We shall now discuss the points of distinction and of agreement between these alpha-, and beta-automaticities.

The principal feature of an automatic, periodic movement is its tempo, which in its turn depends again on the so-called refractory stage inserted into every period. Now this tempo is determined by the amount of radio-activity for the alpha-group, as well as for the beta-group. A minimum amount is required for the movements to reveal themselves at all, and a maximum quantum that should on no account be surpassed. This allows a certain latitude for dosages, which is narrow for the alpha-, and broad for the beta-group.

Somewhere in this latitude there is a point of greatest frequency, the optimum. This point being established for the two sorts of rays, the frequencies will be the same for either group.

Such an investigation evidently requires a constant temperature. It is also clear that, when the temperature is variable the two determining factors: amount of radio-active matter and degree of the temperature, may cooperate or counteract each other. It has already been shown that there is a law, which determines these relations, but I do not intend to enter into it here. Now, when both for potassium and for uranium the optimum doses have been found, which yield the highest frequency, the frequencies for potassium- and for uranium-automaticity are equal. This is instanced in Fig. 1. In the centre the potassium-beat is shown, separated to the right and to the left by a standstill from two other pulsations; these two other pulsations represent the paradoxical phenomenon appearing when passing from perfect potassium-dosis to a perfect uranium-dosis, and conversely ¹⁾. To the right and to the left the uranium-beat can be observed. Its frequency does not differ from that of the automaticity in the centre of the figure.

Another property the two automaticities have in common is a

¹⁾ These Proceedings Vol. XIX, p. 1043, (1917) C.R. Soc. de Biol. t. 84 p. 704. Paris 1921.

similar need for radio-activity in the several subdivisions of the heart. This is seen best when passing from a perfect uranium-dosis

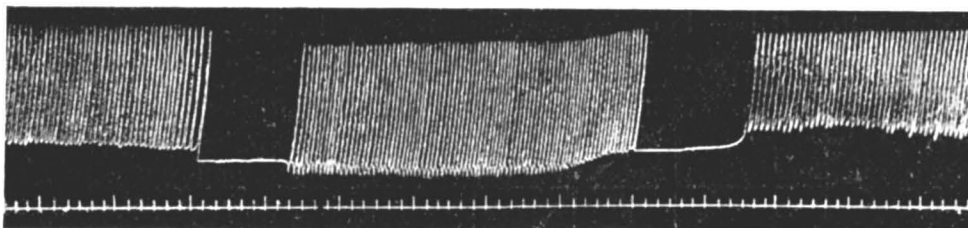


Fig. 1.

Frog's heart KRONECKER's canula 14° C., red light.

Transition from a circulating fluid with 25 mgr. uranyl nitrate to another with 300 mgr. potassiumchlorid per litre, and then back again to 25 mgr. uranyl nitrate. The transitions generally took place resp. 40 and 60 seconds before the paradoxical standstills, indicated in the figure by a white line. Potassium pulsation in the centre. Time $\frac{1}{6}$ min.

to a perfect potassium-dosis or the reverse with a simultaneous registration of the sinus, atrium, ventricle. If no conductive disturbances occur, it will be seen that the three divisions of the heart will stand still and resume their beats at the same moment with automaticities of their own. This is illustrated below in fig. 2 for an eel-heart in situ, which was perfused first with a uranium-liquid and at a moment designated in the time-line by *S* with a potassium-liquid.

The phenomenon, instanced in fig. 2 requires, however, accurate dosage of uranium as well as of potassium. It would not be surprising, if inaccuracy in this respect should engender dromotropism.

A third property the two automaticities have in common is the self-regulation after extrasystole, for α -conditions as complete as for the β -conditions.

The fourth common property is the initial similarity of the alpha- and the beta-electrogram, though I must admit that afterwards a difference may come forth through secondary influences¹⁾.

Only in adventitious respects do the two automaticities differ.

Of the greatest importance in this respect is the tonicities of the heart. The conditions determining the auto-tonus of the cardiac muscle are:

¹⁾ Klinische Wochenschrift Jahrg. I N°. 12 (or Diss. H. SLOOFF, Utrecht 4 July 1922).

- a. the number of calcium-ions placed or not placed over against univalent-ions.
- b. the number of H-ions.
- c. the amount of light incident upon the heart, especially in the presence of a fluorescent substance.

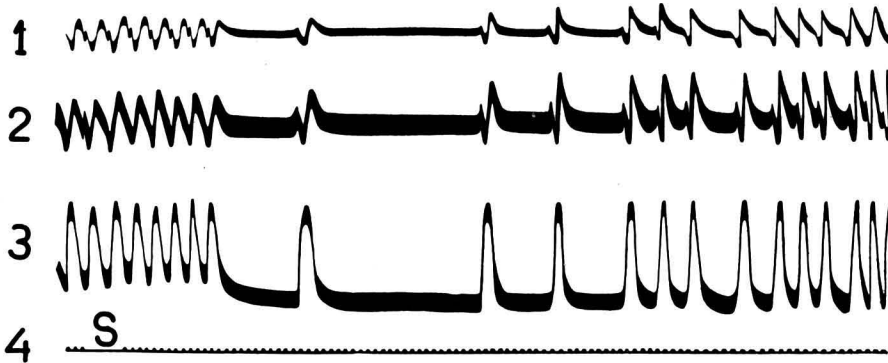


Fig. 2.

Eel's heart in situ. Perfusion from vena cava, first with a circulating fluid, containing 15 mgr. thorium-nitrate per litre, then with a circulating fluid, containing 100 mgr potassium-nitrate. 1 sinus, 2 atrium, 3 ventricle. Time in sec. At S transition from one fluid (thorium-beat) to the other (potassium-beat). Only in the ventricle a light tonus is noticeable during the thorium-beat. It has disappeared already for the greater part in the first beat performed by the heart during the paradoxon.

When applying uranium as an α -rayer each of the three above conditions is modified. Sub *a* undergoes a change because over against the calcium-ion not only univalent ions are placed, but also uranyl. Sub *b* is modified, because a solution of uranyl-salt causes a small increase of H-ions in Ringer's solution. True, this factor may be eliminated by the addition of a trace of CaCO_3 , but let it be supposed that this did not take place. Sub *c* has been modified, because in the organ perfused with a potassium-fluid the incident light has only an inappreciable influence unless its strength be enormous, while in the presence of a fluorescent uranium-liquid also ordinary light will show its tonic action.

It will, therefore, be considered quite rational that in fig. 1 the bases of the uranium-elevations are not so low as those of the potassium-elevations. When thorium is substituted for uranium the phenomenon is less pronounced, still, it is certain that even then the tonus is not quite absent.

With emanation-beats¹⁾ and with pulsation evoked by outside radiations with polonium, there is often some increase of tonus,

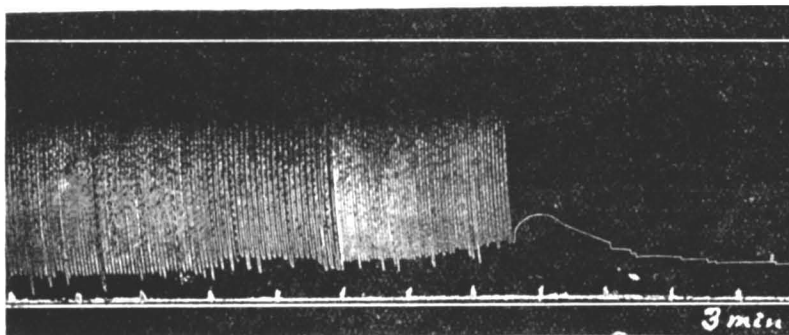


Fig. 3.

Frog's heart, KRONECKER's cannula.

Deprived for some hours by potassium-free perfusion of diffusing potassium and of part of the depot. Then pulsating during the night with 100 mgr. of potassium-chlorid per litre. Next morning standstill with potassium-free Ringer's mixture. Recovery of pulsation due to omnilateral polonium radiation. At the beginning of the curve the polonium was taken away.

Nearly half an hour later the polonium-beats cease. They had caused no increase of tonus worth mentioning.

which need not surprise us if we consider what has been stated sub *a*. Increase of tonus, however, is not a typical feature of alpha-automaticity, since it can exist without this increase when it is brought about from the outside by polonium-radiation. This is illustrated in Fig. 3²⁾. A heart that after cautious, prolonged perfusion with potassium-free Ringer's solution, had been deprived of a considerable portion of its potassium depot, continued pulsating for a long time also when subjected from the outside to omnilateral polonium-radiation. These pulsations occur without additional increase of tonus. The polonium is taken away at the beginning of the figure.

Besides in the tonus-condition, the two automaticities are also distinguished in the relation of the regularly pulsating hearts to the action of the constant current, to the alternating current and to diathermy. These distinctions have been described by Dr. DEN BOER³⁾ in his Thesis, so that I will not revert to them.

¹⁾ ZWAARDEMAKER and T. P. FEENSTRA, C. R. Soc. de biologie, t. 84, p. 377. Paris 1921. ZWAARDEMAKER, Klin. Wochenschr. Jahrg. I, N^o. 11. 1922. Arch. intern. de Physiol. vol. 18, p. 284, 1921.

²⁾ Another instance is given by ZWAARDEMAKER and G. GRIJNS, Arch. néerland. de physiol. t. 2, p. 502, 1918.

³⁾ M. DEN BOER, Dissertation. Utrecht 1 Maart 1921.

The heart has served us as a type of the two automaticities; the natural one depending on the radio-activity of potassium, or rubidium, and the artificial one, that can be evoked by the radio-activity of uranium, thorium, ionium, radium, emanation. In quite the same way there is a mutual resemblance between the alpha- and beta-automaticities of the gut and the uterus.
