In the last term of (17) we may consider (β) to be constant and so we have

$$-\varkappa^2 \sum_i \frac{m_i}{r_i} \sum_{j \neq i} \frac{m_j}{r_{ij}},$$

where r_{ij} represents the distance of the i-th body from the j-th.

We so obtain

$$g_{44} = 1 - \varkappa \sum_i \frac{m_i}{r_i} + \tfrac{1}{2}\varkappa^2 \left(\sum_i \frac{m_i}{r_i}\right)^2 - 2\varkappa \sum_i \frac{m_i v_i^2}{r_i} - \tfrac{1}{2}\varkappa \sum_i m_i \ddot{r}_i - \varkappa^2 \sum_i \frac{m_i}{r_i} \sum_{j \neq i} \frac{m_j}{r_{ij}}$$

Putting

$$\varkappa m_i = 2\, k_i,$$

we have

$$\left.\begin{aligned} ds^2 = & \left(1 - 2\sum_i \frac{k_i}{r_i} + 2\left(\sum_i \frac{k_i}{r_i}\right)^2 - 4\sum_i \frac{k_i v_i^2}{r_i} - \sum k_i \ddot{r} - 4\sum_i \frac{k_i}{r_i} \sum_j \frac{k_j}{r_{ij}}\right) dt^2 \\ & + 8\sum_i \frac{k_i}{r_i}(\dot{x}_i dx + \dot{y}_i dy + \dot{z}_i dz) dt - \left(1 + 2\sum_i \frac{k_i}{r_i}\right)(dx^2 + dy^2 + dz^2) \end{aligned}\right\} \quad (18)$$

where j in the last term of g_{44} does not take the value i.

This is the field required.

Physiology. — "*Researches on the function of the sinus venosus of the frog's heart*". By E. BROUWER. (Communicated by Prof. HAMBURGER).

(Communicated in the meeting of May 27, 1916).

I. *Effect of $CaCl_2$, KCl, NaCl and osmotic pressure.*

Introduction.

As we know the myogenous theory of the heart supposes the impulse to the automatic motion of the heart to originate in the muscular substance of the sinus venosus. There must be a centre there whence the rhytmic stimulus takes its origin, which stimulus is transmitted through auricle and ventricle. From a chemical point of view there is no longer anything mysterious about the occurrence of such periodical stimuli, since BREDIG has made us acquainted with the periodical contact-catalysis.

The reader will remember his experiment: a mercury-surface is covered with a solution of hydrogenperoxyde. A red layer of HgO is formed, but after a short time it disappears and O_2 being set free, a pure mercury-surface is the result. This phenomenon is repeated rhythmically.

Now it must be esteemed of the greatest importance to get acquainted with the chemism of the stimulus originating in the sinus venosus.

These considerations induced Prof. HAMBURGER to suggest that I should *enter upon a systematic investigation of the effect of various chemical and physico-chemical agents on the place of the chemism and their effect, restricting myself to the sinus venosus.*

The effect of salts and other substances on the heart as a whole, has indeed been investigated, but the matter then becomes too complicated to enable us to arrive at conclusions as regards the chemism of the sinus. The conclusions drawn from the study of the isolated ventricle or the auricle-ventricle system too cannot be immediately applied to the sinus. (See also summary on p. 464). In this connection I may quote the opinions of HERING and SAKAI as regards KCl. The former supposes that with respect to the frequency the "nomotope" centres are inversely proportionate with the "heterotope" ones. He supposes that KCl has a stimulating effect on certain "heterotope" centres [1]). SAKAI on the other hand supposes that the sinus is stimulated into greater frequency by KCl.

Method of Investigation.

After some fruitless attempts to register the contractions of the *isolated* sinus, I have made use of ENGELMANN's suspension-method. The fluid was driven through the heart from the vena cava inf. behind (below) the liver, mainly as suggested by MINES. The following modification, however, seems to me of some importance. Besides one or both of the aortas also both venae cavae sup. were cut through at some distance from the auricle, so that the fluid could also flow away through these. If this is not done, blood will remain in the veins long after the experiment has begun. This must affect the frequency. If the fluid passing through the heart impedes automatism, such a vein will retain its former rhythm. Every contraction of the vein is transmitted to the auricle, which will, therefore, beat faster than if auricle and veins had been in contact everywhere with the same perfusion fluid.

The difficulty is that auricle and ventricle are not supplied with so much fluid, and may under certain circumstances determine the rhythm, this can, however, be easily ascertained. Though I have constantly paid attention to this, I have observed it but seldom. The curves relating to these experiments have of course not been used for this publication.

When the heart of large esculents had thus been treated, the pericardium parietale was removed, the frenulum was cut through,

[1]) By "nomotope" centres HERING (Centralbl. f. Phys. Vol. 19. 1905, p. 129) means the places, from which the normal stimulus originates; "heterotope" centres are those from which it originates in abnormal conditions.

the ventricle was carefully turned up and, if necessary, fixed by a piece of wadding.

The parietes of the sinus then lying bare were taken with a small "serre fine", which transmitted the contractions by means of a very light lever to the sooted paper, so that they were magnified about ten times. Special care was taken that the other parts of the heart should either not modify the curves at all or modify them but slightly. This can be done very easily.

As a perfusion fluid I used a solution of RINGER containing: 0,6 % NaCl, 0,0075 % KCl, 0,01 % $NaHCO_3$, whilst the $CaCl_2$ percentage was in the first experiments 0,01 % $CaCl_2$ 6 aq. and afterwards 0.01 % $CaCl_2$. without crystallization water: that is about twice as much. [The $CaCl_2$ solution obtained by weighing the crystallized salt was titrated afterwards]. This fluid was gradually modified in accordance with the nature of the experiments. The percentage of $NaHCO_3$ remained the same, however, to prevent changes into $H^{\cdot}$ and OH'.

The deviations obtained on the sooted paper varied from 1 to 5 millimetres and were also during the experiments highly variable, thus forming a contrast with the frequency. The latter decreased a little at first, but when the heart had once become hypodynamic, it remained surprisingly regular; also when after a series of other fluids, the original solution was taken again, the frequency returned entirely or almost entirely to its former value.

In this connection it may be noticed that for the heart-action the automatism of the auricle is of much greater importance than its contractility.

Tonus-fluctuations have been observed but seldom.

$CaCl_2$.

The diagrams I and II relate to the experiments with $CaCl_2$.

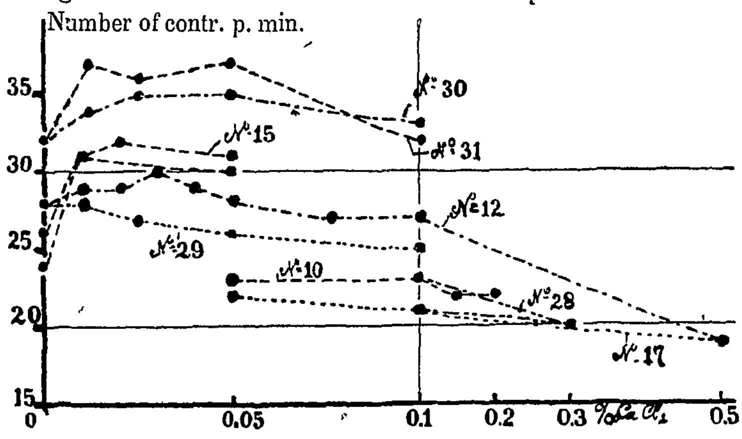


Diagram I. Effect of $CaCl_2$ on the frequency of the sinus venosus; dose from 0 to 0.5 ‰.

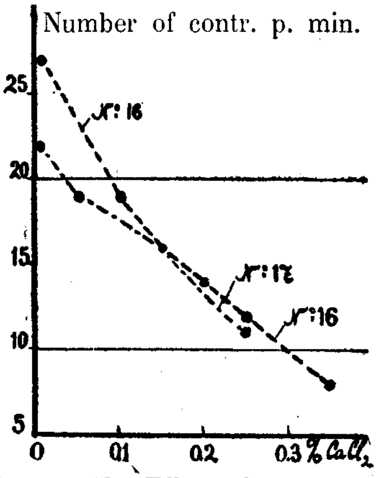


Diagram II. Effect of excessive dose of $CaCl_2$ on the frequency of the sinus venosus.

They show that the concentration of the salt was gradually increased or decreased. Before passing on to another stage I waited till the frequency had become constant. Mostly this was already the case after 15 minutes except with weak concentrations. A return from low to high concentrations resulted in a rapid modification of the frequency (fig. 1).

In these as in the following experiments the temperature varied between 13° and 17°, but was the same during each experiment.

Increase of the $CaCl_2$ percentage

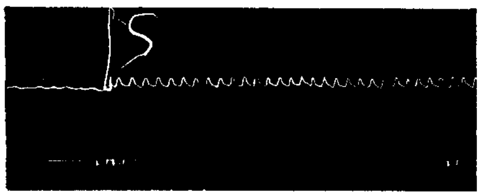


Fig. 1. Transition at once from RINGER's fluid without $CaCl_2$ to the same fluid with 0.005 % $CaCl_2$. Effect after 5 min. Time denoted in min.

of the perfusion fluid resulted in a slow but uniform decrease of the *frequency* (fig. 2), which lasted until the contraction-height became imperceptible.

The *deviation* increased distinctly at first (fig. 2) and decreased regularly afterwards. In the two experiments with high concentrations the contractility had disappeared at $\pm$ 0.3 % $CaCl_2$.

The maximum contractility can of course not be determined with accuracy from these experiments. Probably it is not far from 0.1 % $CaCl_2$.

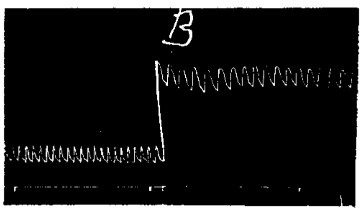


Fig. 2. Transition from RINGER's fluid with 0.005 % $CaCl_2$ to the same fluid with 0.1 % $CaCl_2$. Effect after 5 min. Time denoted in half minutes.

The *tonus* increases. This was not observed regularly, probably owing to the diminutive size of the object and its delicate structure. At the highest concentration, however, the sinus was strongly contracted whilst the limp veins had contracted into threads in which there was hardly a lumen visible.

The osmotic pressure not being kept at the same height during the experiments, its influence was studied separately afterwards. The modification effected by it amounted to 3 beats per minute at most.

Decrease of the $CaCl_2$ *percentage*

caused an increased *frequency*, which was small indeed, but was met with in all the experiments.

A very remarkable fact was that from a certain concentration upwards the frequency hardly ever (diagr. I) increased any longer, but decreased, and that sometimes rather much.

When the concentration had arrived at 0, the sinus stopped entirely after a shorter or longer time.

The fact is that the points of the diagrams at $CaCl_2 = 0\%$ have no right of existence. Therefore it should be expressly stated that they were noted down as long as it was barely possible to count the contractions or when at least the fluid containing no $CaCl_2$ had for a long time been driven through the sinus. The latter also holds good for the diagrams on KCl (III and IV).

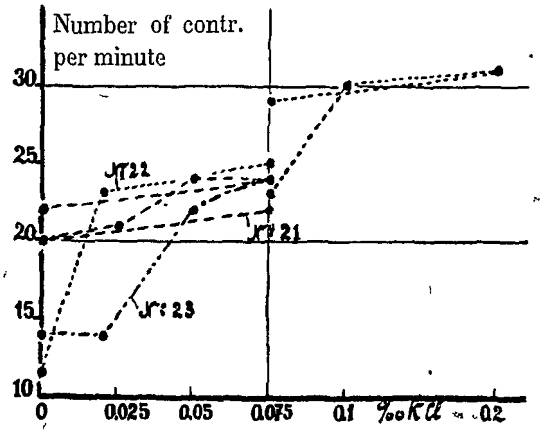


Diagram III. Effect of KCl on the frequency of the sinus venosus. $CaCl_2$ 6 aq. = 0.01 %.

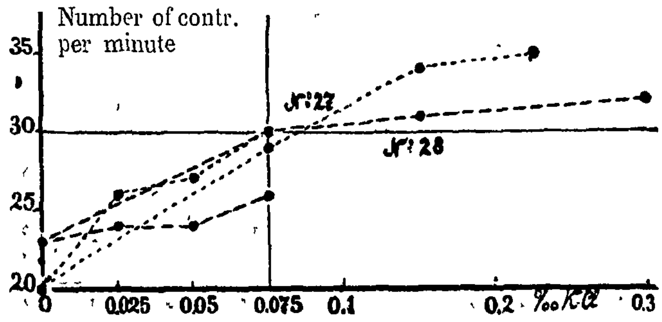


Diagram IV. Effect of KCl on the frequency of the sinus venosus. $CaCl_2$ (without water of crystallization) = 0.01 %.

Moreover some experiments were made on the withdrawal of all $CaCl_2$ at once. Here too we obtained — though not always - first an increased frequency, which was followed by a decrease.

Number 17. 28—1—16 t = 13° Rana esculenta, experiment with the sinus venosus; both venae cavae sup. and one of the aortas cut through, the other one tied off.

After some other fluids:

2.40. RINGER being led through, number of contractions per min.: 22.

2.44. RINGER without $CaCl_2$. Number of contractions per minute: after 5′: 24: after 10′: 24; after 15′: 22; after 20′: 22; after 25′: 22; after 30′: 23; after 45′: 21; after 50′: 22; after 55′: 21; after 60′: 21.

3.16. led through: RINGER. Frequency per minute after 5′: 22; after 10′: 22; after 15′: 22.

As regards *deviation* and *tonus* the former regularly decreased to 0; the latter did not always manifest itself in the curves, but likewise tends to a decrease.

Hence the sinus and ventricle automatism differ considerably as regards frequency. The sinus is retarded by an addition of $CaCl_2$ to the physiological doses, the ventricle is stimulated into greater frequency, likewise retarded, however, in higher concentrations. The difference may perhaps after all be reduced to a difference in degree, for starting from RINGER's solution without $CaCl_2$ I observed when I passed on to a weak concentration, a more rapid rhythm also of the sinus, but at higher concentration a smaller frequency again. The difference is that the maximum frequency for the sinus lies below the physiological concentration of $CaCl_2$ and that for the ventricle above it. This makes it clear why they may behave differently at or near the usual concentration.

KCl.

The diagrams III and IV relate to the *frequency* when the quantities of KCl are changed. In III we had 0.01 °/₀ of $CaCl_2$ 6 aq and in IV 0.01 °/₀ $CaCl_2$ without water of crystallization. See also fig. 3.

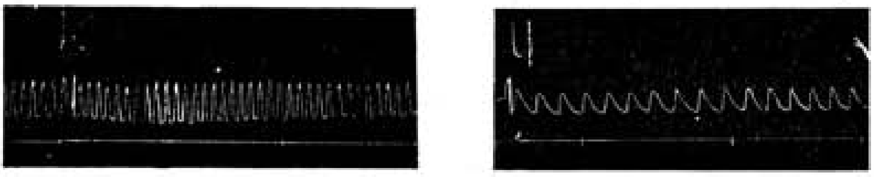


Fig 3. Retardation of the rhythm by withdrawal of KCl. At K RINGER flowed through. At U (70′ after K; the last quantity of KCl had been withdrawn for 40′. Time marked in half minutes.

An increased KCl percentage caused an increased *frequency* until the contractions became too slight to be registered, whilst a decreased KCl perc. resulted in a decreased frequency,

Hence under the action of KCl the sinus likewise behaves in a manner directly opposite to that effected by $CaCl_2$; the differences in the diagrams are, however, more pronounced. No reasons have been found hitherto which may justify the conclusion that, also with regard to KCl, there is only a difference in degree between auricle and ventricle.

Just as with $CaCl_2$ the *contractility* did not differ from that of the ventricle. It decreased at an increased KCl percentage and could hardly be registered already in diagram III at 0.02 °/₀ and in diagram IV at 0.03 °/₀. A decrease of the KCl percentage, however, caused it to increase. When a solution containing no KCl was led through the sinus, the contractions became indeed smaller after the process had lasted for hours, but they never disappeared, so that it cannot be determined from these experiments whether KCl is absolutely necessary for the sinus-automatism.

Further the experiments gave an impression that the sinus as a rule responded more slowly to changes in the concentration of the KCl than of the $CaCl_2$. To concentration changes of the NaCl it mostly responded more quickly than to changes in the $CaCl_2$ percentage.

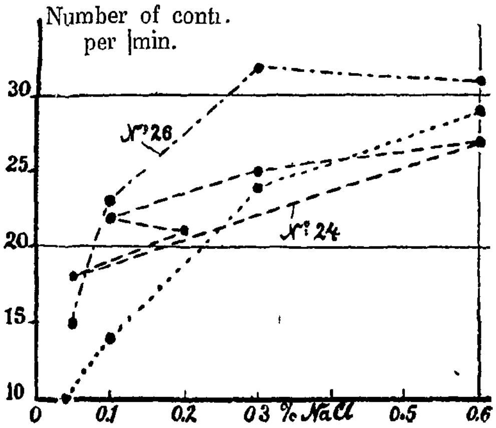
As regards the *tonus* it was discovered that, just as with the ventricles, it decreased when the KCl perc. was raised and increased when it was lowered.

NaCl.

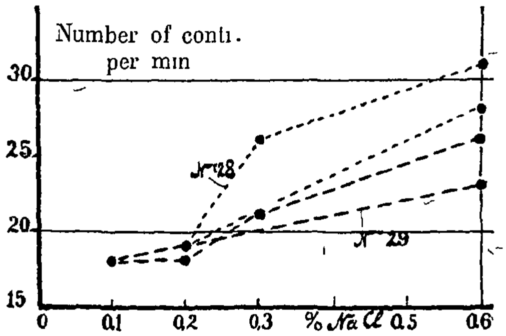
The decrease of concentration caused by NaCl was investigated only while the osmotic pressure was kept constant by means of cane-sugar.

Again the frequency was directly opposite to that of the isolated ventricle, as appears from the diagrams V, where 0.01 °/₀ of $CaCl_2$ 6 aq had been added, and VI where 0.01 °/₀ without aq. was used. See also fig. 4. When the amount of $CaCl_2$ was small, greater quantities of NaCl could be withdrawn than when it was greater. If the concentration was weaker than the minimum values marked on the diagrams or even equal to 0, then the concentrations stopped within a few minutes, which makes a great difference with KCl and $CaCl_2$.

The *contraction-height* mostly increased a little at first; then it



Diagr. V
Decrease of the NaCl %, the osmotic pressure being kept constant by cane sugar. Effect upon the frequency. $CaCl_2$ 6 aq = 0,01 %.



Diagr. VI
Decrease of the NaCl %, the osmotic pressure being kept constant by cane-sugar. Effect on the frequency. $CaCl_2$ (without water of crystallisation) = 0,01 %

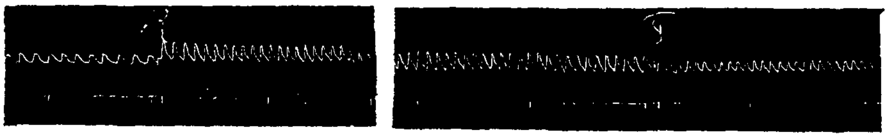


Fig. 4. Effect of NaCl. At R change from NaCl 0,1 % to NaCl 0,3 %. Effect after 5 minutes. At T of the same experiment, change from NaCl 0,3 % to ordinary Ringer. Effect after 5′. Time marked in half minutes.

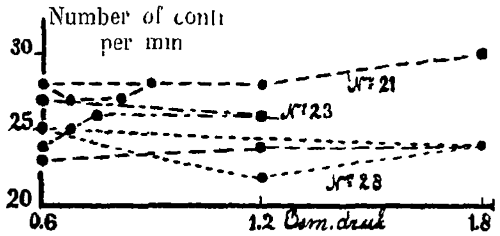
strongly decreased between 0.3 % and 0.1 % (fig. 4). To what extent the increase must be attributed to the cane-sugar or to the withdrawal of NaCl as such, cannot be stated with certainty.

On the *tonus* I have only a few observations in two experiments. In both experiments it increased when NaCl was withdrawn, whilst a return to the original quantity of NaCl caused a decrease.

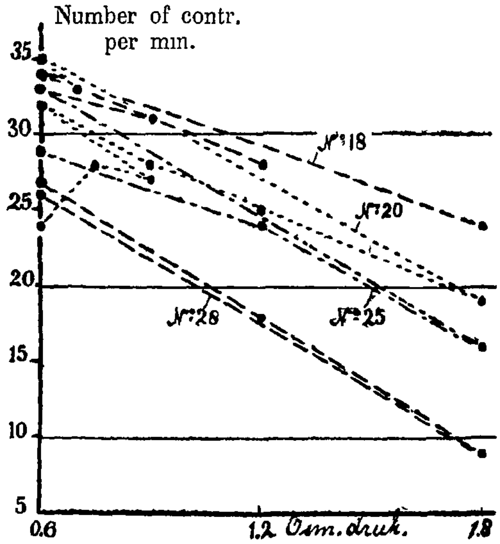
Increase of osmotic pressure by cane sugar and urea.

Glucose was precluded, its action on the heart being too specific. This is according to most authors not the case with cane-sugar, and urea was taken because, in contrast with other tissues it is marked, according to LUSSANNA, by a certain osmotic activity as regards the heart.

A comparison of the diagram VII and VIII brings to light the great difference: cane-sugar decreases the *frequency*, urea does not alter it in the least. In order to be absolutely certain we have sub-



Osm druk = Osm. pressure.
Diagram VII.
Effect of an increased osmotic pressure on the frequency of the sinus venosus with *urea*.
Osmotic pressure expressed in $^0/_0$ NaCl



Osm druk = Osm pressure
Diagram VIII
Effect of an increased osmotic pressure on the frequency of the sinus venosus with *canesugar*
Osmotic pressure expressed in $^0/_0$ NaCl

mitted the same sinus successively to the action of cane-sugar and urea (N° 28) and again we obtained the same result

Now it may be looked upon as certain that cane-sugar will be osmotically active as regards the muscular fibres of the sinus

The fact that urea shows so little activity in such a strong concentration, thus differing so much from a substance possessing osmotic activity, suggests the conclusion that the muscle fibres of the sinus are permeable $CO(NH_2)_2$ If this is the case, an addition of urea must cause a withdrawal of water — and consequently a smaller

Number 29; 24—3—16, t = 14°; 10.50 h R. esculenta; sinus venosus perfused.
Cut through both aortae and both venae cavae sup.
The experiment was continued at 25-3-16 and summarised as follows.

Letter on the curve	Time	Fluid	Number of contr. per 1′ after		Osmotic pressure in % NaCl	Remarks
			5′	10′		
L′	11.30	Ringer	before the exp. 23		0.6	t = 13°
M′ N′	11.33	Ringer + urea	21	24	1 2	
Q′ P′	11.47	Ringer + urea	23	24	1.8	
Q′ R′	11.58	Ringer	26	25	0.6	

frequency — before the ultimate quantity has been diffused. It was found that in nearly all the experiments the number of contractions had indeed decreased somewhat after 5′, and had reached its original value again after 10′ or 15′. (See table p. 463).

In weak concentrations the effect of both substances on the *excursion* was a favourable one; in greater concentrations it was now favourable, now unfavourable.

The effect on the *tonus* was so little pronounced that we must abstain from expressing an opinion on the subject.

Summary.

From these experiments it appears that there is indeed *a great difference between the sinus and the isolated ventricle of the frog; they behave in directly opposite ways, as regards frequency under the influence of $CaCl_2$, KCl and NaCl.*

When the physiological dose is increased KCl heightens and $CaCl_2$ lowers the frequency.

When the physiological dose is diminished $CaCl_2$ slightly raises the frequency, and KCl and NaCl retard it.

The fact that a copious withdrawal of $CaCl_2$ mostly lowers the frequency led to the supposition that the different behaviour of sinus and ventricle towards this salt, is merely a difference in degree. These facts were not observed in the case of KCl and NaCl.

Tonus and deflection are like those of the ventricle. A slight increase of the $CaCl_2$ perc. of RINGER's fluid has a positive inotropic effect; with great quantities the effect is negative inotropic. The tonus is always raised.

An increase of the KCl percentage has a negative inotropic effect and lowers the tonus.

A decrease of the $CaCl_2$ percentage likewise lowers the tonus and results in a negative inotropic effect.

A decrease of the KCl percentage has a positive inotropic effect and increases the tonus.

A slight decrease of the NaCl percentage results perhaps in a positive inotropic, a great decrease in a negative one. Probably the tonus is heightened.

An increase of osmotic pressure by means of cane-sugar gives negative inotropic results, a quantity of urea with the same osmotic pressure leaves the frequency the same. It is highly probable that the muscular cells of the sinus are permeable to urea.

Further it appeared from these experiments that of frequency, tonus and deflection the former is by far the most constant.

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Astronomy. — *"Contributions towards the determination of geographical positions on the West coast of Africa"* IV. By C. Sanders. (Communicated by Prof. E. F. van de Sande Bakhuyzen).

(Communicated in the meeting of June 24, 1916).

1. *Introduction.*

My last paper [1]) on my determinations of geographical positions on the West coast of Africa dates from 1908; I describe there what I did in that direction in the years 1903—1906. In 1906 I was in Europe for some time, but in May 1907 I had returned to Chiloango, while in the mean time my stock of instruments had been augmented by a Zeiss telescope of 80 mm. aperture and 120 cm. focal distance. The principal purpose for which I had obtained this telescope was to be able to observe occultations of stars by the moon, in order in this way to improve my results for the absolute longitude of Chiloango, which I had previously determined by means of lunar altitudes. At the same time I wished to try to make other observations, which might be of use scientifically, my especial aim being the observations of eclipses and other phenomena of the satellites of Jupiter; while, when the telescope had only been in my possession for a short time, I had an opportunity of observing the transit of Mercury on Nov. 14th 1907, at least partially. I published the result of these observations in 1908 [2]). At the same time, some of the observations, especially those of the reappearance in occultations, were made very difficult by the circumstance that my telescope had provisionally been provided with an azimuthal mounting, which was to be replaced later by a parallactic one. This proved, however, to be difficult to accomplish and finally I ordered a second telescope exactly the same as the first, but mounted parallactically.

1) C. Sanders. Bijdragen tot de astronomische plaatsbepaling op de Westkust van Afrika. (III). Versl. Akad. Amst. **17**, 66—84. 1908. (Proceedings XI. p. 88).

2) C. Sanders. Waarneming van den overgang van Mercurius . . . . Versl. Akad. Amst. **17**, 84—85. 1908. (Proceedings XI. p. 108).