Selbstverständlich beziehen sich die angeführten Einwände nur auf die Deutung der Experimente von Yeagley, die ohne Zweifel die Grundlage für eine abgeänderte Theorie bilden können.

Summary

A survey is given of recent work on physical aspects of sensory processes. The reasoning which leads to the generally recognized view that one rod of the retina is excited by only one quantum of light is given in par. II. In par. III a summary is given of the papers by Hecht and Van der Velden on the number of rods which must be struck in order to obtain *a sensation* of light. Par. III describes the role of the quantum character of light at higher intensities (de Vries), where it sets a limit to intensity discrimination and visual acuity. The influence of Brownian movement on the process of hearing is discussed in par. VI. It is found that the Brownian movement of the inner ear is close to the threshold actually observed (de Vries), whereas the Brownian motion of the air at the eardrum (see Sivian and White) is below the audible threshold. The role of the Brownian movement *in* the sense cells is described in par. VII; the results are used for an analysis of the mechanism of hearing (see also de Vries); evidence is obtained that electric voltages are generated in the tectorial membrane (the well-known cochlear microphonics) and that they play an important part in the mechanism of energy transfer to the sense cells (similar voltages were also derived from the cupolæ in the lateral lines of fishes by the present author). Finally some physical arguments are sumarized against Yeagley's theory of bird navigation.

Conduction, Automaticity, and Tonus of Visceral Muscles

By Emil Bozler[1], Columbus, Ohio

To those who are interested in the precise measurements of physiological changes, a piece of intestine may appear as a poor object of study. However, a study of this type of muscle is indispensable for our understanding of the function of numerous organs, and promises an insight into some general problems, such as the mechanism of initiation of spontaneous contractions (automaticity), and the nature of the action of many drugs. These are some of the problems which we shall discuss in the following pages on the basis of recent investigations.

It is unlikely that the study of a single organ provides all the clues necessary for the successful study of the complex muscular activity of the viscera. It is essential for such a task to study as many different types of muscles as possible in order to determine their fundamental properties.

Indeed, there is a great diversity in the physiological characteristics of muscles. Generally, they are classified according to histological criteria into striated and smooth muscles. Physiologically, however, it is more significant to distinguish between "multi-unit" muscles and visceral muscles[2]. The former, which include skeletal muscles and the muscles of blood vessels, are normally activated by the central nervous system and consist of numerous independent units. The latter, which include the heart and the smooth muscle of many visceral organs, possess automaticity, behave like single units, and have also other properties in common. While the muscles of blood vessels generally belong to the first of these two groups, Mislin's[1,2] observations suggest that the spontaneously beating, non-innervated veins of the bat's wings belong to the second category. It is evident, therefore, that smooth museles fall into two widely different catogories.

I. *The unitary character of visceral smooth muscle*

We shall be concerned here chiefly with the smooth muscle of the viscera. Their activity generally consists of waves of contraction. The first problem which arises, therefore, is the mechanism of conduction in this type of muscle. It can be studied most conveniently in the ureter, but similar studies have been made with the intestine and the uterus[3].

If the ureter is stimulated by a single weak electric shock of sufficient duration, a wave of excitation travels with equal velocity in both directions. The response originates at the cathode, it strictly obeys the all-or-none law, and is followed by a long refractory phase. Thus, except for the time factor, the responses of the organ agree exactly with those of cardiac muscle. This expresses itself also in the action potentials. In their simplest form, diphasic potentials show R and T waves like those of cardiac muscle, and monophasic potentials have a long plateau (Fig. 1, *A* and *B*).

In view of these similarities, it seems reasonable to assume that the mechanism of conduction is fundamentally the same in the ureter and the heart. The ureter, therefore, may be considered as a muscular unit, a view originally proposed by Engelmann[4].

[1] Department of Physiology, The Ohio State University, Columbus.
[2] E. Bozler, Biol. Symp. *3*, 95 (1941).

[1] H. Mislin and M. Kauffmann, Rev. suisse Zool. *54*, 240 (1947).
[2] H. Mislin, Exper. *4*, fasc. 1, 28 (1948).
[3] E. Bozler, Am. J. Physiol. *122*, 614 (1938).
[4] T. W. Engelmann, Pflüger's Arch. *3*, 248 (1870).

Moreover, a theoretical consideration of the responses shows that the electric properties of the organs are incompatible with the assumption that the muscle fibers are independent units and that conduction is due to a nervous mechanism. This result is confirmed by the observation that the responses of the ureter are not abolished by cocain and nicotine in concentrations which paralyse all known nervous mechanisms[1].

While the responses of visceral smooth muscles fundamentally are very simple, normal activity often is very complex. Even a casual knowledge of the movements of the intestine and the uterus proves that the function of their muscles cannot be understood by merely considering them as large muscular units. We shall see, however, that many of their functions can be explained on the basis of classical muscle physiology
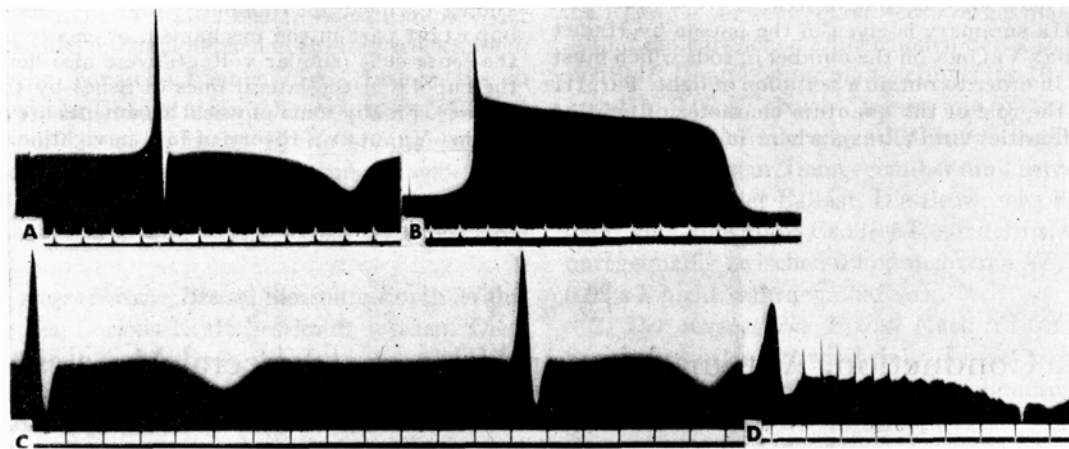

Fig. 1. *Action potentials of visceral smooth muscles. A* diphasic, *B* monophasic potential of the rat's ureter. Time $^1/_5$ sec, *C* diphasic potential of the stomach of the dog, *D* same for the cat. Time 1 sec.

It may be difficult for some biologists to accept this conclusion because, histologically, anastomoses between the muscle fibers have not been demonstrated convincingly. This may be due to the small dimensions of the structures concerned. The demonstration of anastomoses, however, is not of decisive importance. From a physiological standpoint a membrane is not necessarily a physiological barrier. Thus the giant fibers of the earthworm behave, with regard to action potentials and the effects of electric currents, like single nerve fibers[2], although they are divided into distinct segments by transverse membranes. These membranes evidently are not electrically polarizable and for this reason are not acting as a barrier for the conduction of impulses. The same may be true for the cell surfaces separating smooth muscle fibers.

Under suitable conditions, results like those just described for the ureter can be obtained also with muscles from the uterus and intestine. The similarity in the underlying mechanisms is well demonstrated by the action potentials of these organs. Thus the stomach and small intestine[3], during weak rhythmic activity, give almost exactly the same action potentials as the ureter and the heart (Fig. 1 C). It is true, however, that, in some cases, in addition to the sustained potentials brief spikes appear during strong contractions, a phenomenon which thus far has not been explained (Fig. 1 D).

if some additional factors are taken into consideration[1].

(1) Muscular excitability varies widely under different physiological conditions. This is well illustrated by the change in the properties of uterine muscle during the estrous cycle[2]. During anestrus the muscle is practically inexcitable and excitability reaches its peak during the height of estrus. In an animal in anestrus this change can be induced by the injection of an estrogenic substance. For several days after the beginning of this treatment the threshold to electric stimuli gradually drops. While excitability is low the responses are only local but when excitability has become sufficiently high the responses are conducted over the whole muscle as in the ureter, and the all-or-none law can then be demonstrated as readily as in a piece of cardiac muscle. This change in the properties of the muscle is responsible for the marked change in the character of the normal spontaneous movements of the organ. During anestrus they are weak and highly incoordinated, whereas strong contractions of the whole organ occur during estrus.

Adrenaline and sympathetic nerve impulses likewise have a striking effect on excitability. In most organs, they lower electric excitability, often so ·much that muscular conduction is temporarily abolished[3]. This effect on excitability is the basis of the well-known inhibitory effect of the sympathetic nervous system on the motility of some viscera.

[1] E. Bozler, Am. J. Physiol. *122*, 614 (1938).
[2] E. Bozler, unpublished.
[3] E. Bozler, Am. J. Physiol. *144*, 693 (1945).

[1] E. Bozler, Biol. Symp. *3*, 95 (1941).
[2] E. Bozler, Endocrinology *29*, 225 (1941).
[3] E. Bozler, Am. J. Physiol. *130*, 627 (1940).

Still another factor is the refractory phase which follows each contraction and lasts for many seconds. This partly accounts for the low electric excitability of muscles which are continuously in a state of rhythmic activity.

Normally, muscular excitability is low in many types of visceral smooth muscles. Responses, therefore, are generally not conducted over long distances, and different parts of an organ can be active independently. For this reason, not because of any fundamental difference from other types of muscles, the all-or-none law has, in practice, only a limited applicability for many visceral smooth muscles.

(2) The nervous system can influence the excitability of visceral muscles through the extrinsic nerves, as we have just seen. The intestine has, in addition, an intrinsic nervous system which is important in the coordination of muscular activity. This complex problem will be touched here only briefly.

If an object is introduced into the intestine it is usually transported in a caudal direction. The muscular activity responsible for this transport is generally called a "peristaltic contraction", but this term is ambiguous and even misleading. This problem can be studied most conveniently in the duodenum, of the dog. Direct observation and records of action potentials[1] show that the content of the intestine is pushed forward by strong rhythmic contractions on the oral side. The individual contractions may travel in a caudal or oral direction. Thus the "peristaltic contraction" actually is an advancing front of strong rhythmic activity.

The response of the intestine just described can be shown to be controlled by an enteric reflex mechanism. The reflex is normally initiated by mild mechanical stimulation, such as stroking the mucosa, or stretching. The nerve impulses are conducted over a synaptic pathway, chiefly in an oral direction, increasing the strength of rhythmic contractions, particularly those of the circular muscle. This response is essentially the myenteric reflex of the older investigators. However, no evidence for a wave of inhibition distal to the region stimulated was found. Furthermore, the reflex generally does not initiate contractions but merely increases the strength of rhythmic activity which is usually present in empty organs. We have to distinguish, therefore, between the individual contractions which are spontaneous and are conducted within the muscle and the wave of increased activity which is controlled by the enteric nervous system.

The responses just described should be sharply distinguished from the so-called peristaltic contractions of the ureter and the stomach. The latter are single contractions and there is no evidence that they involve any nervous mechanism. They are resistant to high concentrations of drugs which paralyze all known nervous elements. Thus the peristalsis of the isolated ureter is not abolished by nicotine and cocain in concentrations as high as 1:100 and the movements of the stomach continue under the influence of the highest concentrations of nicotine tolerated by an intact animal. On the contrary, the myenteric reflex and the transport of a bolus are abolished by very low concentrations of nicotine.

II. The initiation of spontaneous activity

The rhythmic activity of visceral muscles continues with little change after complete separation from the central nervous system. This phenomenon has been known for a long time for the heart. The question of the initiation of its beat has given rise to many investigations and speculations but the first actual information on the mechanism of this phenomenon was obtained by electrical methods.

This problem can be studied conveniently in the ureter. Impulses arise at the proximal end of this organ. Now, if one lead is placed on the pacemaker and another one or more centimeters away, it can be observed that each spontaneously arising impulse is preceded by a slowly rising negativity which is strongest at the pacemaker itself and is absent at a distance of a few millimeters[1]. When this local potential reaches a critical magnitude it initiates an all-or-none conducted wave of contraction.

Sometimes, instead of these exponentially rising local potentials, the discharge of a conducted response is preceded by sinusoid oscillations of gradually rising amplitude. Impulses arise from the negative peaks of these local potentials, and are usually discharged in bursts separated by long periods of rest, a phenomenon well known for cardiac muscle and designated as Luciani periods. Since this type of rhythm is abnormal and is generally not found in fresh muscles, the exponentially rising local potentials must be considered to be responsible for normal automaticity.

After these observations were made on the ureter it seemed suggestive to study the heart in a similar manner. The results obtained confirmed that the beat of the heart is initiated in the same manner as in the ureter[2]. In the sinus venosus of the turtle, recording monophasic potentials, a weak slowly rising potential precedes the conducted impulse (Fig. 2 B). In injured cardiac muscle, oscillatory potentials of gradually rising amplitude, like those described for the ureter, often lead up to the discharge of a group of impulses, giving rise to Luciani periods (Fig. 2 D).

The role of local potentials for the initiation of impulses is shown also by another phenomenon. Each cardiac impulse is generally followed by a prolonged after-potential which can be positive or negative depending on the conditions. If the muscle is treated with

[1] E. Bozler, unpublished.

[1] E. Bozler, Am. J. Physiol. 136, 543 (1942).
[2] E. Bozler, Am. J. Physiol. 138, 273 (1943).

a solution containing a large amount of calcium ions the after-potential becomes oscillatory and, if the oscillations are strong enough, they lead to the discharge of impulses[1]. In ventricular muscle, which ordinarily does not discharge spontaneously, these after-potentials may maintain a regular spontaneous discharge for a period of time.

amount of tension is the smaller the slower its response. By the myothermic method of A. V. Hill, the heat production during a maintained contraction could be measured in an adductor muscle of a snail[1]. The smooth muscle was found to be 30 to 180 times more economical than frog's skeletal muscle, a difference which is fully accounted for by the difference in the time relations
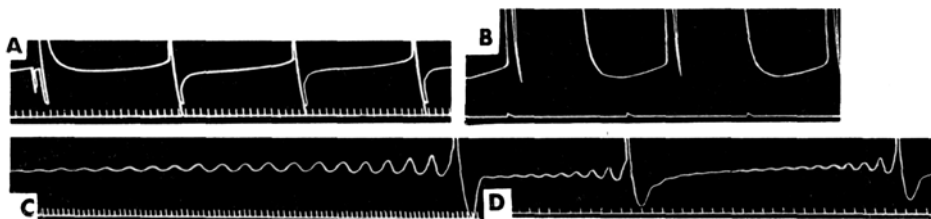

Fig. 2. *Local potentials initiating Impulses*. *A* ureter of cat, slow potential rise previous to each spontaneous impulse; first impulse elicited by electric shock. *B* sinus venosus of turtle, monophasic, one lead on pacemaker. *C* and *D* oscillatory potentials of ureter and sinus venosus of turtle resp. Time 1 sec.

The local oscillatory potentials, although they do not occur under normal conditions, are a remarkable phenomenon because they seem to be tied up with some very fundamental properties of the tissues. This is suggested by the fact that their frequency varies very little between different preparations and is not influenced by injury or drugs. Adrenaline and acetylcholine change their magnitude but not their frequency.

It is interesting that similar local potentials have been observed also in other types of tissue, in the snail's heart and in nerve fibers, by Arvanitaki[2] and others. In tissues not normally possessing automaticity, like the nerve fibers, oscillatory potentials can be evoked in Ca^{++} free solutions but they have a frequency several hundred times greater than that of smooth muscles.

III. Tonus

The term tonus is generally used to describe the fluctuating level of tension or length on which brief contractions may be superimposed. The term is poorly defined but has been most useful to physiologists, as shown by its frequent use. In the following, an attempt will be made to clarify this concept in the light of recent investigations.

It has frequently been assumed that tonus is due to a contractile mechanism entirely different from that responsible for the fast contractions. Thus, Parnas and Bethe[3] claimed that a state of tension can be maintained by smooth muscles without a rise in metabolism. This conclusion was based on the observation that some of these muscles could remain contracted much longer than would be possible for a skeletal muscle. It has been shown, however, that the energy expenditure of a muscle required to maintain a certain

of contraction. Therefore, a strong tension can be maintained by smooth muscles at a rate of metabolism which is of the same order of magnitude as the resting metabolism and is small in comparison with the metabolism of the whole animal. The ability of some smooth muscles to remain contracted for long periods without fatigue, therefore, does not require the assumption of any mechanism different from that of the tetanic contraction. In fact, beeause the responses of all smooth muscles which have been studied adequately differ from striated muscle only quantitatively, it seems inconceivable that they can remain contracted without continuous energy expenditure.

Since the term tonus is generally used descriptively, we should not expect that we are dealing with a single mechanism. Actually, it can be shown that several physiological changes can be responsible for variations in tonus.

In a few instances, muscles contain two types of muscle tissue, a fast and a slow component. A well-known example is the adductor muscle of *Pecten* and other molluscs which consist of a striated portion making possible rapid movements of the shell and a smooth muscle which can keep the shell closed for long periods and is responsible for tonus. In the turtle's heart, the well-known tonus waves are due to a separate layer of smooth muscle. A peculiar situation exists in the smooth muscle fibers of chromatophores of cephalopodes[2] where the activity of each fiber can be directly observed and recorded. Each of these fibers is capable of contracting and relaxing slowly and of responding to electric shocks by rapid twitches. There is evidence that these two types of contractions, which can be carried out independently, are due to different types of fibrils in the same muscle fiber.

[1] E. Bozler, Am. J. Physiol. *139*, 477 (1943).

[2] A. Arvanitaki, Propr. rythm. de la matière vivante, Paris 1938.

[3] J. Parnas, Pflügers Arch. 134, 441 (1910) – A. Bethe, ibid. 142, 291 (1911).

[1] E. Bozler, J. Physiol. *69*, 442 (1930).

[2] E. Bozler, Z. vergl. Physiol. *13*, 762 (1931).

A simple situation is presented by the tonus changes of rhythmically active organs like the intestine. There the term tonus is used to describe the changing length or tension on which the contractions are superimposed. That this depends chiefly on the completeness of relaxation following each contraction is suggested by the observation that, in general, tonus rises when the strength of contraction increases and vice versa.

result of previous activity, of distension, or the action of drugs. That actively maintained tension exists in the resting muscle is shown by the observation that, in the ureter and cardiac muscle, tension may temporarily drop below the previous level following a response (Fig. 3 *B*). This was also found true for turtle skeletal muscle[1] but the possibility that a weak tetanic contraction of some of the muscle fibers has existed before
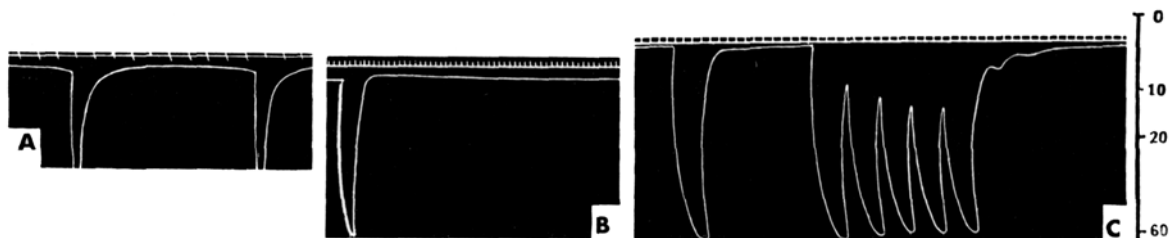

Fig. 3. *Tonus changes in tissues obeying the all-or-none law.* A slow rise in tension preceding the conducted response in dog's ureter, corresponding to the local potential Fig. 1 *A*. *B* Pressure in the isolated turtle ventricle drops below previous resting pressure following a response, or it may oscillate as in *C*. Scale mm Hg. Time 1 sec.

A persistent weak contraction can be due to asynchronous activity of different parts of a muscle. This condition can exist also in visceral muscles if excitability is too low to permit conduction of impulses over long distances and it gives rise to irregular weak action potentials[1].

The mechanisms of tonic contraction mentioned so far have no great general interest, but recent studies have revealed one type of tonus change essentially different from the tetanic response. It has been found that the non-conducted potentials described above are associated with weak mechanical changes, a rise in negativity producing contraction, and positivity being accompanied by relaxation. Thus, in the ureter, a weak contraction gradually develops previous to the discharge of an impulse in the region of the pacemaker. The oscillatory potentials also are accompanied by corresponding mechanical changes (Fig. 3).

It must be emphasized that these tonus changes were observed under conditions where the all-or-none law was strictly valid. Consequently the phenomenon cannot be explained as being due to the discharge of a limited number of the muscle fibers.

While the tonus associated with local potentials can be sharply distinguished from contractions due to conducted impulses there is no reason to assume that it is caused by a different type of contractile mechanism or that it does not involve energy changes. The close parallelism between tension and potential in the "resting" muscle can best be understood on the assumption that the resting metabolism of a muscle leads to the active production of tension just like the activity metabolism, the difference being merely quantitative. We may conclude, therefore, that, in visceral muscles, the resting metabolism fluctuates spontaneously or as a

stimulation and has temporarily ceased after the response cannot be ruled out with certainty in this case.

The mechanical effects produced by variations in the resting metabolism can be expected to differ greatly in different muscles. From data on the energy expenditure for maintaining tension and the resting heat production[2], and assuming that the efficiency is the same as in tetanic contractions, it can be computed that a frog's sartorius muscle could produce a tension of only 30 mg with its own resting metabolism. This tension naturally could not be easily distinguished from passive tension and changes, such as might be expected under physiological conditions, would be so small that they could be determined only with great difficulty. In slower muscles, for the reasons given above, the tension produced by the resting metabolism would be higher. Therefore, in smooth muscle, this tension would be at least 30 times greater than in a frog's muscle.

By the term tonus one often implies some type of maintained contraction essentially different from a tetanic contraction. One might, therefore, be inclined to restrict its use to the slow non-conducted mechanical changes described above. However, usually, it is not possible to evaluate the contributions of various mechanisms in the production of a maintained contraction. It seems, therefore, more practical to use the term in a purely descriptive manner and to qualify it in cases which have been analyzed. I propose the term "resting tonus" for the mechanical changes associated with the local potentials, since it represents a resting condition and its magnitude is related to the resting potential.

Whether the resting potential is large enough in smooth muscle to be mechanically significant for the

[1] E. Bozler, Biol. Symp. *3*, 95 (1941).

[1] E. Bozler, unpublished.
[2] E. Bozler, J. Physiol. *69*, 442 (1930).

function of visceral organs is uncertain. At present, greater interest attaches to its relation to automaticity, which has been discussed above. The fact that the initiation of impulses is associated with mechanical changes is interesting also in another respect. Potential changes are often considered purely as surface phenomena, but in our case the associated tonus changes show that also the interior of the cell is involved. Depolarization of the cell surface probably is the direct cause of the discharge of impulses but it must, in turn, be due to a change in metabolism. This leads to the conclusion that the chemical processes of tissues possessing automaticity fluctuate spontaneously and, under certain conditions, undergo sinusoid oscillations at a frequency characteristic for each type of tissue.

In conclusion: the smooth muscles of visceral organs are muscular units. This result is based on a study of conducted responses, on action potentials and other characteristics which are very similar to those of cardiac muscle. The peculiarities of smooth muscles are largely due to the slowness of the response and the variability of excitability. The latter is influenced by such factors as hormones, extrinsic nerve impulses, and, in the intestine, also by an intrinsic nervous system. Spontaneous contractions are initiated by a gradually developing, non-propagated activity which manifests itself in a potential change and a rise in "tonus". The term tonus as ordinarily used does not represent any distinct contractile mechanism. Tonus is produced in smooth muscle by several physiological changes. There is no evidence that it can be caused by a contractile mechanism different from that responsible for phasic contractions.

Résumé

Les muscles lisses des Vertébrés appartiennent à deux catégories: ceux des viscères, lesquels ont une fonction automatique, et ceux qui comme les muscles des vaisseaux sanguins sont innervés par les nerfs moteurs. Les propriétés physiologiques des muscles lisses viscéraux sont très semblables à celles du muscle cardiaque ainsi que l'a montré l'étude de la conduction, du potentiel d'action et des effets du courant électrique. Les particularités des muscles lisses viscéraux tiennent en grande partie à la lenteur de leur réaction et aux fluctuations que présente leur excitabilité. Cette dernière est influencée par des facteurs tels que des hormones, des excitations transmises par les nerfs extrinsèques et, dans le cas de l'intestin, par le système nerveux intrinsèque. Les contractions spontanées débutent par une activité locale qui augmente lentement et se manifeste par un changement du potentiel et un accroissement du «tonus». Le tonus se produit dans les muscles lisses par diverses modifications de l'état physiologique. Rien ne prouve qu'il soit provoqué par un mécanisme essentiellement différent de celui des contractions rapides.

Brèves communications – Kurze Mitteilungen
Brevi comunicazioni – Brief Reports

Eine Näherungsformel
für die Prämie der Invalidenversicherung

Wird das Ausscheiden der aktiven Versicherten durch die Intensität der Sterblichkeit μ^a_{x+t} und die Intensität der Invalidierung ν_{x+t} gemessen, bedeutet ferner μ^i_{x+t} die Sterbeintensität der Invaliden und a^i_x den Barwert der laufenden Invalidenrente «1», so ist die kontinuierlich zu entrichtende Prämie für die anwartschaftliche, höchstens bis zum Alter von $x + n$ Jahren stetig zahlbare Invalidenrente «1» gegeben durch

$$P^i_{x\overline{n}|} = \frac{\int_0^n e^{-\delta t}\, l^{aa}_{x+t}\, \nu_{x+t}\, a^i_{x+t:\overline{n-t}|}\, dt}{\int_0^n e^{-\delta t}\, l^{aa}_{x+t}\, dt} \, , \tag{1}$$

oder was dasselbe ist, durch

$$P^i_{x\overline{n}|} = \frac{\int_0^n e^{-\delta t} \int_0^t l^{aa}_{x+\tau}\, \nu_{x+\tau}\, \frac{l^i_{x+t}}{l^i_{x+\tau}}\, d\tau\, dt}{\int_0^n e^{-\delta t}\, l^{aa}_{x+t}\, dt} \tag{2}$$

mit

$$l^{aa}_{x+t} = l^{aa}_x\, e^{-\int_0^t (\mu^a_{x+\tau} + \nu_{x+\tau})\, d\tau}$$

und

$$l^i_{x+t} = l^i_x\, e^{-\int_0^t \mu^i_{x+\tau}\, d\tau} \, .$$

Bei der numerischen Auswertung von (1) wird in letzter Zeit die Aktivitätsordnung l^{aa}_{x+t} meist durch die Überlebensordnung l_{x+t} ersetzt[1] und die Sterblichkeit der In-

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[1] Vgl.: M. Jacob, Atti del decimo Congresso internazionale degli Attuari, t. 1, p. 304 (1934). – G. Trier, Skand. Aktuarietidskr. *29*, 143 (1946). – Vereinigung schweiz. Lebensversicherungsgesellschaften, Technische Grundlagen und Bruttotarife für Gruppenversicherungen, 1948.