

## The early years of Excitable Media from Electro-Physiology to Physical-Chemistry

Jean-Jacques Perraud  
Centre de Recherche Paul Pascal / C.N.R.S.  
Av. A. Schweitzer, F-33600 Pessac, France.  
e-mail : [imaperraud@crpp.u.bordeaux.fr](mailto:imaperraud@crpp.u.bordeaux.fr)

### Abstract

A short historical survey of electro-physiology is proposed here. Beginning with Galvani's works in the middle of the XVIII<sup>th</sup> century, this subfield of Science slowly brought closer to physical-chemistry during the XX<sup>th</sup> century. New tools of research were imagined. This evolution seems to be linked to the development of research in the field of chemical and biochemical oscillators.

Only a few years after Petrus Van Musschenbroek had built about 1745 this strange bottle, the so called "Bottle of Leyde", several scientists began to study the effects of electricity on living systems. As early as 1756 in Bologna, Leopoldo Caldani noticed the action of an electric discharge on heart and muscles. In those years, Father Nollet, an abbot and one of the first science popularizer, startled once 180 royal guards, and 700 monks later. In 1772, after a series of experiments performed in La Rochelle (France), John Walsh demonstrated the electrical origin of the shock generated by the numb-fish or torpedo. Less than twenty years later, the effect of electric spark on frog muscles were described by Luigi Galvani. He noticed that contractions of the frog leg can be obtained without any spark, but only with contacts of a wire made of two different metals. He concluded that a kind of electric discharge or electric currents can be produced by living nerves or muscles. Galvani's interpretation of the phenomenon was severely criticized by his student Alessandro Volta. The latter showed that the electromotive force was generated at the contact points of living tissues and metals, in almost all Galvani's experiments. This was, on one hand the origin of the quite famous quarrel between Galvani and Volta, and on the other hand, the beginning of a new field of research which can be called electro-physiology.

During the nineteenth century, the number of works in the field of electro-physiology grew faster and faster but for a long time, frog leg was still the most sensitive detector for brief electric pulses. The use of sensitive enough galvanometers appeared in the middle of the century. The first experimental evidence that nerves and muscles are capable of generating electromotive forces by themselves has been attributed to Carlo Matteucci and Emil Du Bois Reymond. The latter performed a long series of experiments and tried to study the propagation of brief-lasting electrical stimuli along nerves. But, his monitoring devices were actually not rapid enough to reveal the essential character of the course. Even during the last years of the century, it was impossible to obtain good records of electric activity of nerves and muscles. Ludimar Hermann and Julius Bernstein worked very hard to show that the electric activity can be considered as electric discharges lasting only a few thousands of seconds.

According to Hermann, an excited nerve produced a current which may be able to restimulate adjacent parts of the fiber. Then, the excitation propagate from point to point. The nineteenth century physiologists fully appreciated the essence of the two outstanding properties of nerves, excitability by electric currents and production of electric currents by excitation. The role of the membrane of the cells was discovered later. The discrimination of the ionic permeability of the membrane is actually of great physiological importance. The relative permeability of the membrane to inorganic ions like sodium, potassium and chloride was suggested by Wilhelm Ostwald in 1890. Then, in 1902, Bernstein was the first to consider Ostwald hypothesis in terms of physico-chemical explanation of electro-physiological phenomena. These ideas were discussed between 1890 and 1900.

Everybody should know that Ostwald was not a physiologist but is considered as the initiator of physical chemistry. He occupied the chair of physical chemistry at the University of Leipzig where he created a celebrated research school. One of his most famous students was Hermann Nerst. Quite independantely of his physiological remarks, Wilhelm Ostwald discovered in 1899 a very strange phenomenon during the dissolution of chromium in a concentrated solution of sulfuric acid. He noticed that hydrogen was evolving periodically from the solution, around the metallic sample. During the process, the chromium surface changed periodically of aspect, from dark to brilliant metallic aspect. He recorded the time periodic evolution of hydrogen with a "Chemograph" of his invention. Other metals, like iron, were found to behave in the same way. The next year, Ostwald asked one of his student, Eberhard Brauer, to continue this work. Brauer later married Ostwald's daughter. Brauer showed that the metallic sample exhibits rhythmical changes of potential during the reaction. Using a long iron wire, Ostwald also noticed that the dark coating of oxidation propagates like pulses along the wire. Under slightly different conditions, a single pulse of oxidation can be obtained only by touching the wire with a zinc needle. The close analogy of this electrochemical pulse and the propagation of the impulse on a long nerve axon stroke to Ostwald. He suggested to another student, Henry Heathcote, to investigate more thoroughly the analogy with excitability in nerves, but Heathcote's work did not receive any attention from physiologists.

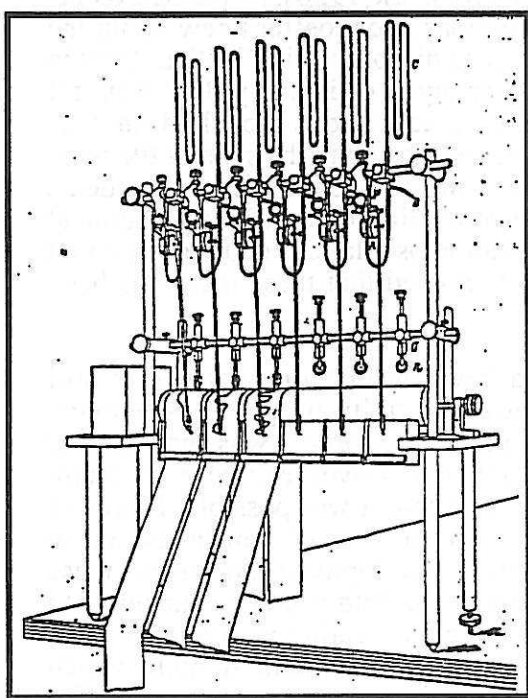


Figure 1 :

Ostwald's chemograph.(1900)  
enabled him to record the periodic  
emission of hydrogen above the  
sample of chromium

We owed the renewal of interest for the propagation of oxidation pulses along a iron wire to Ralph Lillie, an american physiologist. He began to study the phenomenon in 1917 or 1918 at Clark University in Worchester. He imagined to use the iron wire as an experimental model of nervous transmission. This model was called "the iron wire Ostwald-Lillie's model". Lillie moved to the University of Chicago and for more than fifteen years (1920 to 1936) Lillie has investigated the behavior of the iron wire model and traced out the many analogies with the excitability of nerves. According to him, electrical polarisation (like electrotonus), changes in temperature, variations in the composition of the medium, surface-active compounds (like narcosis) affect activation and transmission of oxidation pulses. He also showed the existence of a refractory state with a progressive recovery of the excitability of the iron surface, similar to that of nerve impulse. He also considered that the rhythmic emission of waves is another analogy with living systems like cardiac muscle. With a ring of iron, Lillie mimicked the observations of G. R. Mines on a muscular tissue cut from a large heart. A pair of waves of excitation are periodically emitted in a point of the ring and travel in opposite directions. They finally annihilate each other when they collide. He mentioned that this type of circular propagation of waves can be at the origin of certain unco-ordinated phenomena of nervous transmission like cardiac fibrillation.

Only a few years later, in 1940, a long series of experiments on the excitability of the "Ostwald-Lillie model" was started, at the Physico-Chemical Institute at the University of Leipzig, the famous institute created by Wilhelm Ostwald in the last years of the nineteenth century. These experiments were carried out at the request of Karl Bonhoeffer. He, too, was interested in the analogy of the phenomenon with excitability in nerve fibers and in the periodic character of the reaction. During the war years, activation of passive iron or other metals in sulfuric acid and nitric acid were studied. Signals of electrodes were displayed on the screen of an oscillograph. Bonhoeffer completed Lillie's observations concerning the activation threshold, the latent period between stimulation and activation, the refractory state and the threshold of intensity of stimulation above which periodic activation is observed. He published several papers on the possible mechanism of periodic oscillating reactions between 1941 and 1948. In the first paper of the series, he showed that there is little differences in the mechanism of chemical oscillations in homogeneous and in heterogeneous systems. Reminding of the models proposed by Alfred Lotka and Vito Volterra in the 1920s, he insisted on the fact that autocatalysis is necessary to obtain oscillations. Bonhoeffer knew about the periodic decomposition of hydrogen peroxide by iodate discovered by William Bray in 1917, but he considered that the homogeneous autocatalysis claimed by Bray was still doubtful. Bonhoeffer presented a theory for periodic activations modelled on self-excitatory electrical oscillations, introducing "variables describing the state of the wire, the degree of activation and the degree of refractoriness". He had several students among them, Ulrich Franck, who continued the modelling of oscillating chemical reactions. Bonhoeffer insisted on the fact that relaxation oscillations could correspond to periodic activations in biological systems and reminded that these ideas has been developped previously by Balthasar Van der Pol.

Lillie's idea that periodic activations play a key role in living systems is still present. The possibility of modelling cardiac muscle activity by physico-chemical phenomena remained in several physiologists mind. The problem was that nobody knew if a wave of activation can propagate or not in a convex excitable medium. According to Garrey's experiments on turtle heart in 1924, it was possible. Pieces of unperforated muscle exhibited closed circuits of activity, which can be linked to fibrillation and tachycardia. At that time, no theoretical development can support these observations and they were discredited. The step up in the field has to be attributed to the famous mathematician Norbert Wiener who was collaborating with the Mexican cardiologist Arturo Rosenblueth. They proposed an extremely simplified model which can exhibit circular vortices of activity in a two dimensionnal excitable medium like cardiac muscle. In their model, the finite duration of the action potential in heart muscle



and the electrotonic coupling of cells were neglected. Bernard Katz imagined something near but the wavelets of activity he described were wandering without particular order. Other developments came from physiologists and cardiologists, like Gordon Moe on discretized models, between 1955 and 1965. One of them, B. Farley reported a particular mode of self-excitatory oscillations in a computed random interconnected nerves network. This mode appeared in the form of continuous rotating spirals. Computational descriptions of tachycardia, cardiac arrhythmia and fibrillation burst during these years but there were still no clear experiments backing up the numerical simulations.

Several mathematicians and biophysicists were working around similar subjects in the very big Institute of Biological Physics in Moscow during the same period. Among them, I. Balakhovsky proposed a more realistic version of Wiener-Rosenblueth model and computed the dynamics of continuous two dimensionnal excitable media. He both obtained rotating waves he called vortices. These waves could rotate around holes and without holes. V. Krinsky developed his model called "Reverberator" and obtained also spirals by numerical computations about 1965. Experimental proofs was badly needed in U.S.S.R. as in the western countries. Then, there was a break in the activity of research because of the institute moved from Moscow to Pushino, a small town one hundred kilometers from Moscow. Krinsky met in Pushino a young post-graduate student named Anatol Zhabotinsky. The latter told Krinsky that he was working on an homogeneous oscillating chemical reaction. The oscillations were periodic and had the characteristics of relaxation oscillations. Krinsky was immediately very interested in using this reaction to realize an homogeneous excitable medium.

*Труды всесоюзного симпозиума  
по колебательным процессам в биологических  
и химических системах.  
Пушино-на-Оке, 21—26 марта 1966 г.*

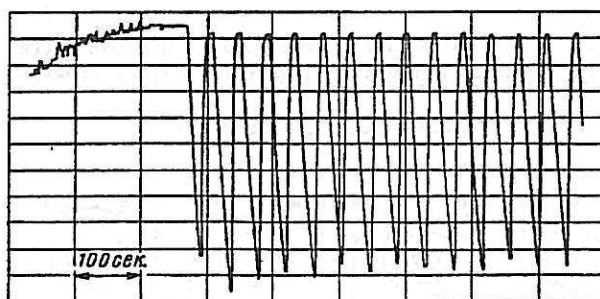


Figure 2 : From Anatol Zhabotinsky's contribution to a symposium on biological and biochemical oscillators in U.S.S.R. in 1966.

The oscillatory reaction Zhabotinsky was working with was known in his institute for several years. Zhabotinsky's thesis was directed by Simon Shnoll, professor Moscow State University. In those years, Shnoll was convinced that oscillating chemical reaction should exist as he was involved in the study of oscillations in complex biochemical systems. He always voiced his opinion to his students. One of them, in the last 1950s, told him that his uncle had already observed an oscillatory chemical reaction. Shnoll immediately wanted to contact the man : Boris Pavlovich Belousov. However, it seems that Belousov refused to meet Shnoll but he sent him the recipe of his reaction and a manuscript of an unpublished article. Shnoll assigned the study of the recipe to several students, including Zhabotinsky. The reaction was the oxidation of citric acid by bromate, catalysed by cerium(IV) in a sulfuric medium. Zhabotinsky obtained the oscillatory behavior and began to write a manuscript during

the spring of 1962. He showed his results to Shnoll and they wrote a letter to Belousov, joining Zhabotinsky's manuscript. Belousov only replied he was glad to see his work continued and gave citation of a published article. Zhabotinsky went to the library to get this publication and included this reference in his thesis dissertation which was nearly completed.

How did Belousov obtain his oscillatory reaction? It is clear that he had no interest about chemical oscillations before. Belousov was only involved in the study of the Krebs cycle. Citric acid is one of the residues of the Krebs cycle. It is produced by condensation of acetic acid with oxalo-acetic acid. Citric acid is degraded in  $\alpha$ -cetoglutaric acid by a mild oxidation. Belousov wanted a chemical tool in order to titrate citric acid. He decided to use bromate because it is a well known mild oxidation agent, but the reaction needed to be catalysed. Then, Belousov added a metal ion as catalyst Ce(IV). The catalysis is efficient only under acid enough conditions, like in sulfuric medium. Belousov noticed that the solution exhibited periodic color changes from yellow to colorless. The phenomenon was striking enough to bring Belousov to undertake a detailed study, including the effects of acidity, of temperature and of initial concentrations of reagents. Some elements of mechanism are even proposed in the first manuscript Belousov submitted. But the paper was rejected for publication and the author went back to laboratory work in order to complete his experimental observations and to improve the mechanism. Safronov suggested him to use a redox indicator like ferroin which enabled to see oscillations in color, from red to clear blue. Nevertheless, the second attempt to publish was another failure because the editor reproached Belousov with the missing of any theoretical explanation of the phenomenon. After several attempts, Belousov became discouraged and forwent publishing until someone heard of his reaction inside the walls of the Institute of Biological Physics, contacted him and induced him to publish a short note in a obscure and strange Journal of References of Radioactive Medecine...which was not refered. The priority of Belousov was then insured and this was the reference Zhabotinsky included in the bibliography of his thesis.

ТРУДЫ ВТОРОГО ВСЕСОЮЗНОГО СИМПОЗИУМА ПО КОЛЕБАТЕЛЬНЫМ  
ПРОЦЕССАМ В БИОЛОГИЧЕСКИХ И ХИМИЧЕСКИХ СИСТЕМАХ  
(23-27 ноября 1970 г.)

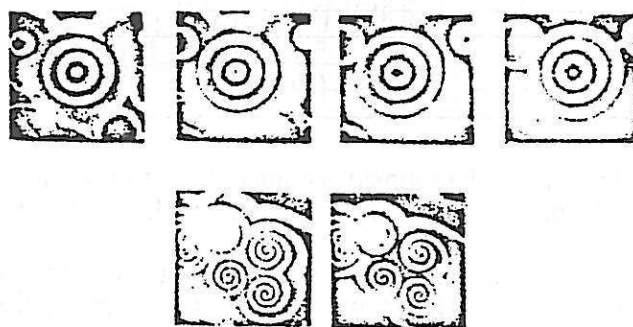


Figure 3 : From Anatol Zhabotinsky's contribution to the second symposium on biological and biochemical oscillators in U.S.S.R. in 1970.

The time oscillatory behavior was not the most interesting thing in Krinsky's mind but the chemical oscillations closely resembled to relaxation oscillations in recorded in electrocardiograms. His idea was to test this reaction in an unstirred quasi two dimensionnal medium in order to see waves and to study their propagation. At that time, Zhabotinsky was collaborating with Alex Zaïkin and V. Vavilin but they failed in

trying to obtain waves. For a long time, only bulk oscillations have been observed until an unskilful student spilled the mixture on the table and forgot it for several minutes. Back to the table, he was astonished at seeing clear blue waves in the red liquid. Rapidly, Zhabotinsky, Zaïkin and Krinsky understood these waves were actually the waves of excitation they were looking for. Waves were periodically emitted from centers and propagated in the medium in the form of concentric circles which are now called "target patterns". Krinsky was still thinking about a rotating wave in an excitable continuous medium and he asked Zhabotinsky if it was possible to break a front of propagation. Zhabotinsky kindly complied and the broken front immediately began to coil itself up and a spiral wave was finally obtained. these results were not published in the western countries, and spiral waves were independantly obtained later by Art Winfree in the United States.

This was the starting point of a large number of investigations on propagation of waves in excitable media. The mechanism of formation of target patterns has been studied intensively in the early 1970s and discussion about the exact essence of the pacemakers is still not closed. Spiral waves has been studied since the early 1970s and they are still rotating in a lot of laboratories. Belousov's reaction is now well known and is usually called Belousov-Zhabotinsky reaction or BZ reaction. It became a very valuable tool of research in the field of understanding excitability in living systems such as cardiac muscle. The study of two dimensionnal properties of the waves propagation led to studies in three dimensionnal media like scroll waves, twisted and knotted waves were obtained by Art Winfree. These phenomena should be compared to similar observations in cardiac activity which are still needed.

Belousov's discovery was also the element that bursted the research in the field of chemical oscillators. Oscillations of concentrations had been observed since the early 1960s in several biochemical systems. Glycolytic oscillations discovered by Britton Chance in 1964 can be mentionned. Scientists in that field were ready to accept the idea of an inorganic chemical oscillator and that is probably the reason why Benno Hess, Britton Chance and others decided to organize a meeting. They wanted to get together scientists of all these different but related fields. This meeting finally took place in Prague, between the 21<sup>th</sup> and the 26<sup>th</sup> of July 1968, two months before the Soviet invasion in Czechoslovakia. A second meeting was organized the next year at Hangö in Finland the 16<sup>th</sup> and 17<sup>th</sup> of August 1969. Zhabotinsky could attend to the first conference and presented for the first time the self excitatory homogeneous oscillating reaction to scientists from the western countries. Unfortunately, he was not allowed by his government to go to Finland the next year.

One can notice that the development of physiology of nerves and muscles began with the discovery of electricity because this latter was the most convenient and efficient tool at the hand of physiologists. Numerous poor frogs had to contribute to scientific research and progress until another tool enabled physiologists to explore new fields. From that beginning and until now physiologists has been looking for experimental models in order to simplify the experiments and to get the basic mechanism of nerve impulse, pulses propagation and even to cardiac muscle functioning and disfunctionings. The "Ostwald-Lillie iron wire" model was the first electrochemical experimental model which behaves with a large number of analogies with nerves and muscles. Several decades later, the so-called BZ reaction became the new fundamental tool because this excitable homogeneous reactive solution materialized what was in physiologists dreams for many years.

#### Acknowledgements

I thank P. De Kepper, J. Boissonade, E. Dulos and A. Pacault for stimulating discussions and encouragement ; and the Centre National de la Recherche Scientifique for travel funds.



## References

- Balakhovsky, I. S.** 1965. Several modes of excitation in excitable tissue. *Biophysics* **10**, 1175-1179.
- Belousov, B. P.** 1958. Oscillation reaction and its mechanism (in russian), *Sbornik Referatov po Radiacioni Medicine*, p. 145 Meeting.
- Bernstein, J.**, 1871. Untersuchungen über die erregungsvorgang im nerven- und muskel systeme, Heidelberg.
- Bernstein, J.** 1902. Untersuchungen zur thermodynamik der bioelektrischen ströme., *Pflügers Arch. Ges. Physiol.*, **92**, 521-562.
- Bonhoeffer, K. F.** 1941. Über die aktivierung von passivem eisen in salpetersäure, *Zeitschr. Elektrochem.* **47**, 2, 147-150.
- Beinert, H. Bonhoeffer K. F.** 1941. Über die passivität des eisens und das Ostwald-Lilliesche modell der nervenleitung, II. *Zeitschr. Elektrochem.* **47**, 6, 441-450., III. *Zeitschr. Elektrochem.* **47**, 7, 536-545.
- Bonhoeffer K. F.** 1948. Über periodische chemische reaktionen. I *Zeitschr. Elektrochem.* **51**, 1, 24-29.
- Bonhoeffer, K. F., Brauer, Elfriede and Langhammer, Günter.** 1948. Über periodische chemische reaktionen. II, *Zeitschr. Elektrochem.* **51**, 1, 29-37.
- Bonhoeffer, K. F., Haase, Vera and Langhammer, Günter.** 1948. Über periodische chemische reaktionen. III, *Zeitschr. Elektrochem.* **52**, 1, 60-67.
- Bonhoeffer, K. F., Langhammer, Günter.** 1948. Über periodische chemische reaktionen. IV, *Zeitschr. Elektrochem.* **52**, 1, 67-72.
- Bonhoeffer, K. F., Gerischer, Heinz.** 1948. Über periodische chemische reaktionen. V, *Zeitschr. Elektrochem.* **52**, 1, 149-160.
- Bonhoeffer, K. F.** 1948. Activation of passive iron as a model for the excitation of nerve., *J. Gen. Physiol.*, **32**, 69-91.
- Brauer, E.** 1901. Über das elektrische verhalten des chroms bei auflösung in säuren., *Zeitschr. f. Phys. Chem.*, **38**, 441-486.
- Bray, W. C.** 1921. A periodic reaction in homogeneous solution and its relation to autocatalysis., *J. Amer. Chem. Soc.* **43**, 1262-1267.
- Caldani, L.** 1757. Sull'insensibilità e irritabilità di alcune parti degli animali. (Bologna), Lettera scritta al chiarissimo sig. Alberto Haller.
- Caldani, L.** 1759. Lettera terza del sig. dott. Leopoldo Marc'Antonio Caldani sopra l'irritabilità e sensitività halleriana (Bologna).
- Caldani, L.** 1767. Riflessioni fisiologiche sopra due dissertazioni del sig. Claudio Nicola Le Cat. (Venice).
- Caldani, L.** 1770. Institutiones physiologiae (Padua).
- Chance, B. and Ghosh A.**, 1964. Oscillations of glycolytic intermediates in yeast cells., *Biochem. Biophys. Res. Commun.*, **16**, 174-181.
- Chance, B., Hess, B. and Betz, A.** 1964. DNPH oscillations in a cell free extract of *S. carlsbergensis*., *Biochem. Biophys. Res. Commun.*, **16**, 182-187.
- Chance, B., Schoener, B. and Elsassee, S.** 1964. Control of the wave form of the oscillations of the reduced pyridine nucleotide level in a cell free extract., *Proc. Natl. Acad. Sci. USA*, **52**, 337-341.
- Chance, B., Pye, E. K. and Higgins, J.** 1967. Wave form generation by enzymatic oscillators. *IEEE Spectrum*, **4**, 79-86.

- Du Bois Reymond, E. H.** 1843. Vorläufiger abriß einer untersuchung über de sogenannten froschstrom und über die elektrischen fische, *Annalen der Physik und Chemie*, **58**, 1-30.
- Du Bois Reymond, E. H.** 1849-1884. Untersuchungen über thierische elektrizität, (Berlin, 2 vols).
- Du Bois Reymond, E. H.** 1875-1877. Abhandlugen zur allgemeinen muskel- und nervenphysik, (Leipzig, 2 vols).
- Farley, B. G.** 1965. A neurol network model and the slow potentials of electrophysiology., *Computers in Biomed. Res.* **1**, 265-294.
- Franck, U. F.** 1973. Oscillatory behavior, excitability, and propagation phenomena on membranes and membranes like interfaces. in: *Biological and Biochemical oscillators*, Chance, B., Pye E. K., Ghosh, A. K. and Hess, B., ed. Acad. Press N.Y. London.
- Galvani, L.** 1791. De viribus electricitatis in motu muscolari commentarius.  
see also : Fulton, J. F. and Cushing, H. 1936. A bibliographic study of the Galvani and Aldini writings on animal electricity., *Annals of Science*, **1**, 239-268.
- Garrey, W. E.** 1924. Auricular fibrillation. *Physiol. Rev.*, **4**, 215-250.
- Heathcote, H.** 1901. Vorlänger bericht über passivierung. Passivität und aktivierung des eisens., *Zeitschr.f. Physik. Chemie*, **37**, 368-373.
- Hermann, L.** 1879. Handb. d. physiol. (m. mehreren und physiologen) 6 Bände, Leipzig.
- Hermann, L.** 1881. Hierin v. herausgeber : Muskelphysiol., 260 p. ; Nervenphysiol., 196 p.
- Hess, B., Brand, K. and Gey, G.** 1964. *Internal. Cong. Biochem. Abstr. N.Y.* p. VI-41.
- Hess, B. and Brand, K.** 1965. in: *Control of energy metabolism*. Chance, B., Estabrook, R. W. and Williamson, J. R. ed., p. 111 Acad. Press N.Y.
- Katz, B.** 1946. *Electrocardiography*. Philadelphia, Lea and Febiger.
- Katz, B.** 1956. *Clinical electrocardiography I: Arrhythmias*, Philadelphia, Lea and Febiger.
- Katz, B.** 1966. *Nerves, muscles and synapses.*, mac graw-hill.
- Krinsky, V. I.** 1964. Spread of excitation in an homogeneous medium (state similar to cardiac fibrillation), in russian, *Biofizika*, **11**, 776-784.
- Krinsky, V. I. and Kholopov, A. V.** 1967. Echo in excitable tissue, in russian, *Biofizika*, **12**, 600-606.
- Krinsky, V. I.** 1968. Fibrillation in excitable media, *Prob.in Cybern.*, **20**, 59-80, in russian.
- Krinsky, V. I.** Interview in Herdecke (near Dortmund), Thursday June 25<sup>th</sup> 1992.
- Lillie, R. S.** 1920. The recovery of transmissivity in passive iron wires as a model of recovery processes in irritable living systems., *J. Gen. Biol.* **3**, 107-128.
- Lillie, R.S.** 1923. *Protoplasmic action and nervous action*. University of Chicago Press.
- Lillie, R.S.** 1925. Factors affecting transmission and recovery in the passive iron nerve model., *J. Gen. Physiol.*, **7**, 473-507.
- Lillie, R.S.** 1936. The passive iron wire model of protoplasmic and nervous transmission and its physiological analogues., *Biol. Rev.*, **16**, 181-209.



- Lotka, A. J. 1910. Contribution to the theory of periodic oscillations., *J. Phys. Chem.*, **14**, 271-275.
- Lotka, A. J. 1920. Undamped oscillations derived from the law of mass action. *J. Amer. Chem. Soc.* **42**, 1595-1599.
- Lotka, A. J. 1925. Elements of Physical Biology., The williams & Wilkins Co., Baltimore.
- Matteucci, C. 1840. Essai sur les phénomènes électriques des animaux. (Paris).
- Matteucci, C. 1844. Traité des phénomènes électro-physiologiques des animaux (Paris)
- Mines, G. R. 1914. On circulating excitations in heart muscles and their possible relation to tachycardia and fibrillation., *Trans. Roy. Soc. Can.*, **4**, 43-53.
- Moe, G. K., Harris, A. S. and Wiggers, C. J. 1941 Analysis of the initiation of fibrillation by electrographic studies., *Amer. J. Physiol.*, **134**, 473-492.
- Moe, G. K. and Abildskov, J. A. 1959. Atrial fibrillation as a self-sustaining arrhythmia independent of focal discharge., *Amer. Heart J.*, **58**, 59-70.
- Moe, G. K. 1962. On the multiple wavelet hypothesis of atrial fibrillation. *Arch. Int. Pharmacodyn.*, **140**, 183-188.
- Moe, G. K., Rheinbolt, G. K. and Abildskov, J. A. 1964. A computer model of atrial fibrillation., *Amer. Heart J.*, **67**, 200-220.
- Ostwald, W. 1899. Periodisch verändliche Reaktionsgeschwindigkeiten. *Physikalische Zeitschrift*, **1**, 87-88.
- Ostwald, W. 1890. Elektrische eigenschaften halbdurchlässiger scheidewände., *Zeitschr. f. Physik. Chemie*, **6**, 71-83.
- Ostwald, W. 1900. Periodische erscheinungen bei der auflösung des chrom in säuren., *Zeitschr. f. Physik. Chemie*, **35**, 33-76 and 204-256.
- Rosenblueth, A.: see Wiener, N.
- Shnoll, S. E. 1961. Oscillation of spontaneous transition amplitude of actomyosin preparations from one state to another during storage., *Biofizika*, **6**, 166-171.
- Shnoll, S. E. 1964. Oscillations of SH group concentration in solutions actomyosin, actin and myosin., *Biofizika*, **9**, 532-534.
- Van der Pol, B. and Van der Mark, 1928, Le battement du coeur considéré comme oscillation de relaxation., *Onde électrique*, **7**, 365-392.
- Vavilin, V. A. 1973. A study of a self-excitatory chemical reaction I., The autonomous system., in: Biological and Biochemical oscillators. p. 71-79. Chance, B., Pye, E. K., Ghosh, A. K. and Hess, B. ed., Acad. Press N. Y., London.
- Volta, A., numerous articles , in Giornale fisico-medico, in Opere, in Epistolario and others.  
see also : Sue, P. 1802. Histoire du Galvanisme (Paris)  
Mauro, A., 1969, The role of the Voltaic pile in the Galvani-Volta controversy. *J. History of Medicine*, **24**, 140-150.
- Volterra, V. 1932. Leçons sur la théorie mathématique de la lutte pour la vie. (Paris).
- Walsh, J. 1773. On the electric property of the Torpedo., *Philos. Trans.*
- Walsh, J. 1774. On the Torpedo found on the coast of England, *Philos. Trans.*
- Winfree, A. T. 1972. Spiral waves of chemical activity., *Science*, **175**, 634-636.
- Winfree, A. T. 1973. Scroll shapes waves of chemical activity. *Science*, **181**, 937-939.

- Winfree, A. T. and Strogatz, S. H. 1983. Singular filaments organize chemical waves in three dimensions 1. Geometrically simple waves., *Physica* 8D, 35-49.  
 2. Twisted waves., *Physica* 9D, 65-80.  
 3. Knotted waves., *Physica* 9D, 333-345.
- Winfree, A. T. and Strogatz, S. H. 1984. Singular filaments organize chemical waves in three dimensions 4. Wave taxonomy., *Physica* 13D, 221-233.
- Winfree, A. T. 1984. The prehistory of the Belousov-Zhabotinsky reaction., *J. Chem. Educ.*, 61, 661-663.
- Winfree, A. T. 1987. When time breaks down., Princeton University Press.
- Wiener, N. and Rosenblueth, A. 1946. The mathematical formulation of the problem of conduction of impulses in a network of connected excitable elements, specifically in cardiac muscle. *Arch. Inst. Cardiol. Mex.* 16, 205-265.
- Zaikin, A. N. and Zhabotinsky, A. M. 1973. A study of a self-excitatory chemical reaction II., Influence of external force., in: Biological and Biochemical oscillators. p. 81-88, Chance, B., Pye, E. K., Ghosh, A. K. and Hess, B. ed., Acad. Press N. Y., London.
- Zaikin, A. N. and Zhabotinsky, A. M. 1970. Concentration wave propagation in two dimensionnal liquid-phase self-oscillating systems., *Nature*, 225, 535-537.
- Zhabotinsky, A. M. 1964. Periodic movement in the oxidation of malonic acid in solution., in russian, *Biofizika* 9 (3), 306-311.
- Zhabotinsky, A. M., 1973, A study of a self-excitatory chemical reaction III., Space behavior., in: Biological and Biochemical oscillators. p. 89-96, Chance, B., Pye, E. K., Ghosh, A. K. and Hess, B. ed., Acad. Press N. Y., London.
- Zhabotinsky, A. M. 1970. Investigations of homogeneous chemical auto-oscillating systems., in russian, Thesis, Pushino U.S.S.R.
- Zhabotinsky, A. M. Interview in Herdecke (near Dortmund), Wednesday June 24<sup>th</sup> 1992.

**See also :**

- Dictionary of Scientific Biography, Charles Scribner's Sons, New-York. 1970.
- Histoire Générale des Sciences. 1964. directed by René Taton, Presses Universitaires de France (Paris).
- Poggendorff Biographisch-Literarisches Handwörterbuch.