In Memory of Peter Läuger 1934–1990

"Kinetic basis of voltage dependence of the Na,K-pump" was the title of Peter Läuger's outstanding contribution to the VI. International Conference on "The Sodium Pump" from September 5–9th 1990 in Woods Hole, Massachusetts. The terms "kinetic basis" and "voltage dependence" are in a way characteristic of Peter Läuger's scientific work. His list of publications comprises a broad range of different topics in the field of membrane science. But the analysis of the mechanisms of electrogenic processes in biomembranes by application of kinetic methods certainly is central to his work. It came as a shock to his many friends all over the world when Peter Läuger died on a mountain tour in Venezuela a few days after the conference. Membrane biophysics has lost one of its prominent representatives.

Peter Läuger was born in 1934 at Lörrach in the southwestern part of Germany. He went to the Humanistische Gymnasium in his home town (1944–1953) and studied chemistry, physics, and mathematics at the universities of Basel and Hamburg. In 1961 he took his Ph.D. in physical chemistry at the University of Basel (Switzerland). Contrary to the usual habit of spending some time abroad, Peter Läuger continued his career at the same institute, which is situated in the neighborhood of his German home town. In 1964 only, he went to the Eduard-Zintl-Institut of the Technische Universität Darmstadt and worked for a relatively short period of time with R. Schlögl who is well known for his activities in the field of transport phenomena. He returned to Basel and took his second academic degree (Habilitation) in 1966. Peter Läuger stayed in Basel as a Privatdozent until 1968, when he accepted the call as a full professor in the Department of Biology at the newly founded University of Konstanz. There, he and his group performed most of the studies for which he obtained general recognition.

Peter Läuger's work was strongly influenced by his teacher Werner Kuhn in Basel. Their joint publications on transport phenomena in membranes (1, 2) may be considered as a starting point for Peter Läuger's later studies on transport through ultrathin biological membranes. It was in Basel too, where he started his investigations on lipid membranes (together with W. Lesslauer, E. Marti, and J. Richter [3]). The technique of forming planar lipid films had been developed by Paul Mueller and his colleagues in 1962 (4). Peter Läuger very early recognized the potential of this artificial membrane system as a means of studying mechanisms of ion transport through biological membranes under well-defined experimental conditions. For this purpose a wide spectrum of different methods was applied in the course of a long term research project entitled "Electrical and Optical Properties of Artificial Lipid Membranes" at the University of Konstanz. Within this project, begun in 1968 and now having lasted for more than two decades, Peter Läuger, together with his co-workers and colleagues, analyzed the behavior of ion carriers, ion channels, and ion pumps in lipid membranes.

The scientific work of Peter Läuger is characterized by a strong connection between theory and experiment. From the beginning of his scientific career he showed an inclination towards theoretical considerations. The various experimental studies were always accompanied by theoretical papers dealing with the general physical concept of the problem in question. Studies on the nonlinearity of current-voltage curves (together with Berthold Neumcke [5]) on the rate theory of ion transport through pores (6), on electrical noise associated with ion transport (7), on the coupling of ion transport through pores and the rotation of bacterial flagella (8, 9), or on the kinetic properties of ion carriers, ion channels, or ion pumps (10, 11) represent only a few examples of his numerous theoretical publications. Peter Läuger certainly was not a theoretician in the strict sense of the term. His contributions were intended to provide a theoretical framework for potential experiments and to serve as a basis for further, more sophisticated analysis by others (such as Eckart Frehland's treatment of membrane noise [12]).

The models used by Peter Läuger were frequently based on rate theory, introduced into the field of membrane transport by Zwolinsky et al. (13). Peter Läuger favored this discrete theory over continuous theories (such as the classical electrodiffusion equation of Nernst and Planck), since the former treatment simplifies the interpretation of experimental data. A further advantage of the rate theory is that diffusion steps as well as chemical reactions or conformational changes of transport proteins are described in the same way, namely as transitions between different system states which are separated by energy barriers.

Transition rates may be determined by applying the methods of chemical kinetics. These techniques also allow discrimination between different models. Peter Läuger rigorously used the possibilities of fast kinetic methods to analyze the mechanisms of ion transport through membranes. He was among the first to transfer the voltage-clamp method, introduced in the study of squid axon (14–16), to planar lipid membranes (17). Though the development and application of the different kinetic techniques to planar lipid films (18) are mainly the work of Peter Läuger's co-workers and colleagues, he often took the initiative. Valuable experimental information about various ion transport systems may also be obtained by analyzing electrical noise. Zingsheim and Neher (19) published the first paper on electrical noise in planar lipid membranes, which was supplemented by a parallel and independent study of Läuger's group (20).

These methods were used to investigate the kinetic behavior of lipophilic ions, of ion carriers of the valinomycin type and of channel-forming peptides such as gramicidin A in lipid membranes (reviewed in references 18 and 21). The analysis of carrier-mediated transport has greatly benefited from the work of George Eisenman's group (22). The studies on the gramicidin channel have been important in discriminating between two alternative channel structures. Both structures are formed by different kinds of gramicidin dimers: Dan Urry (23, 24) proposed that the dimer is formed by a head to head (formyl end to formyl end) association of two single-stranded gramicidin monomers which assume the conformation of a $\beta(\pi_{L,D})$-helix. Veatch et al. (25, 26) on the other hand suggested parallel or antiparallel double-stranded β-helices as a channel structure. Using a series of different analogues of gramicidin A, the head-to-head dimer was found to represent the basic structure of the channel (27).

The last decade of Peter Läuger's work was devoted to ion pumps and cotransport systems. The same types of kinetic models, which were previously developed to describe ion transport mediated by model compounds, were now successfully applied to the more complicated transport structures of biological membranes (28–31). The central question asked by Peter Läuger, however, was still the same: how do the microscopic steps of the complicated reaction schemes underlying ion transport through biological membranes depend on the applied voltage? The final answer, Peter Läuger gave to this fundamental problem may be found in a book manuscript entitled "The Electrogenic Ion Pumps" (32). It was completed a few days before he left for his last conference.

The teacher and lecturer Peter Läuger was held in high esteem. Those who had the chance to listen to one of his numerous contributions at scientific conferences were often impressed by the clarity with which he was able to present even the most complicated phenomena. Students of the life sciences who are familiar with the German language may profit from his art of presentation by reading the introductory textbook on physical chemistry and biophysics written together with his colleagues Gerold Adam and Günther Stark (33).

The private Peter Läuger was very modest. He was a bachelor and devoted himself entirely to his scientific work. He owned neither a television set nor a radio. He often spent his spare time walking in the Alps, which are fortunately situated only a short drive from the University of Konstanz. Peter Läuger loved the alpine flora. Though he professionally dealt with molecules and membranes, he was almost an expert in his knowledge of rare plants, which he gained on his numerous travels around the world. It was on one of these journeys that he lost his life.

Peter Läuger was a prominent membrane biophysicist. His influence on this field was profound. The international community in the field of membrane transport has lost one of its most imaginative members.

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Publications Referred to in the Text

1. Kuhn, W., and P. Läuger. 1962. Direkte Umwandlung der Verdünnungsenergie von Lösungen in elektrische Energie durch ultrafeinporige Membranen. *Helv. Chim. Acta.* 45:21–33.
2. Läuger, P., and W. Kuhn. 1964. Stoff- und Volumentransport durch Membranen mit geladenem elektrischen Gerüst. I. Membranen, deren Porenweite klein ist im Vergleich zur Ausdehnung der Ionenatmosphäre. *Ber. Bunsen-ges. Phys. Chem.* 68:4–19.
3. Läuger, P., W. Lesslauer, E. Marti, and J. Richter. 1967. Electrical properties of bimolecular phospholipid membranes. *Biochim. Biophys. Acta.* 135:20–32.
4. Mueller, P., D. O. Rudin, H. T. Tien, and W. C. Wescott. 1962. Reconstitution of cell membrane structure in vitro and its transformation into an excitable system. *Nature (Lond.).* 194:713–719.
5. Läuger, P., and B. Neumcke. 1973. Theoretical analysis of ion conductance in lipid bilayer membranes. *In* Membranes—A Series of Advances. G. Eisenman, editor. Marcel Dekker, New York. 2:1–59.
6. Läuger, P. 1973. Ion transport through pores: a rate-theory analysis. *Biochim. Biophys. Acta.* 311:423–441.
7. Läuger, P. 1978. Transport noise in membranes: current and voltage fluctuations at equilibrium. *Biochim. Biophys. Acta.* 507:337–349.

8. Läuger, P. 1977. Ion transport and the rotation of bacterial flagella. *Nature (Lond.).* 268:360–362.
9. Läuger, P. 1988. Torque and rotation of the bacterial flagellar motor. *Biophys. J.* 53:53–65.
10. Läuger, P. 1980. Kinetic properties of ion carriers and channels. *J. Membr. Biol.* 57:163–178.
11. Läuger, P. 1984. Thermodynamic and kinetic properties of electrogenic ion pumps. *Biochim. Biophys. Acta.* 779:307–341.
12. Frehland, E. 1982. Stochastic Transport Processes in Discrete Biological Systems. Springer-Verlag, Berlin. 1–163.
13. Zwolinsky, B. J., H. Eyring, and C. Reese. 1949. Diffusion and membrane permeability. *J. Phys. Chem.* 53:1426–1453.
14. Cole, K. S. 1949. Dynamic electrical characteristics of the squid axon. *Arch. Sci. Physiol.* 3:253–258.
15. Marmont, G. 1949. Studies on the axon membrane. I. A new method. *J. Cell Comp. Physiol.* 34:351–382.
16. Hodgkin, A. L., A. F. Huxley, and B. Katz. 1949. Ionic currents underlying activity in the giant axon of the squid. *Arch. Sci. Physiol.* 3:129–150.
17. Ketterer, B., B. Neumcke, and P. Läuger. 1971. Transport mechanism of hydrophobic ions through lipid bilayer membranes. *J. Membr. Biol.* 5:225–245.
18. Läuger, P., R. Benz, G. Stark, E. Bamberg, P. C. Jordan, A. Fahr, and W. Brock. 1981. Relaxation studies of ion transport systems in lipid bilayer membranes. *Q. Rev. Biophys.* 14:513–598.
19. Zingsheim, H. P., and E. Neher. 1974. The equivalence of fluctuation analysis and chemical relaxation measurements: a kinetic study of ion pore formation in thin lipid membranes. *Biophys. Chem.* 2:197–207.
20. Kolb, H.-A., P. Läuger, and E. Bamberg. 1975. Correlation analysis of electrical noise in lipid bilayer membranes: kinetics of gramicidin A channels. *J. Membr. Biol.* 20:133–154.
21. Benz, R., H.-A. Kolb, P. Läuger, and G. Stark. 1989. Ion carriers in planar bilayers: relaxation techniques and noise analysis. *Methods Enzymol.* 171:274–286.
22. Szabo, G., G. Eisenman, R. Laprade, S. M. Ciani, and S. Krasne. 1973. Experimentally observed effects of carriers on the electrical properties of bilayer membranes-equilibrium domain. *In* Membranes—A Series of Advance. G. Eisenman, editor. Marcel Dekker, New York. 2:179–328.
23. Urry, D. W. 1971. The gramicidin A transmembrane channel: a proposed π(L,D) helix. *Proc. Natl. Acad. Sci. USA.* 68:672–676.
24. Urry, D. W. 1972. A molecular theory of ion-conducting channels: a field-dependent transition between conducting and nonconducting conformations. *Proc. Natl. Acad. Sci. USA.* 69:1610–1614.
25. Veatch, W. R., E. T. Fossel, and E. R. Blout. 1974. The conformation of gramicidin A. *Biochemistry.* 13:5249–5256.
26. Veatch, W. R., and E. R. Blout. 1974. The aggregation of gramicidin A in solution. *Biochemistry.* 13:5257–5275.
27. Bamberg, E., H.-J. Apell, H. Alpes, E. Gross, J. L. Morell, J. F. Harbaugh, K. Janko, and P. Läuger. 1978. Ion channels formed by chemical analogs of gramicidin A. *Fed. Proc.* 37:2633–2638.
28. Läuger, P., and H.-J. Apell. 1986. A microscopic model for the current-voltage behavior of the Na,K-pump. *Eur. Biophys. J.* 305–321.
29. Läuger, P., and P. Jauch. 1986. Microscopic description of voltage effects on ion-driven cotransport systems. *J. Membr. Biol.* 91:275–284.
30. Läuger, P., and H.-J. Apell. 1990. Electrogenic transport. *In* Monovalent Cations in Biological Systems. C. A. Pasternak, editor. *CRC* Press, Boca Raton, FL. 59–102.
31. Läuger, P. 1990. Kinetic basis of voltage dependence of the Na,K-pump. *In* The Sodium Pump. P. DeWeer and J. H. Kaplan, editors. The Rockefeller University Press. In press.
32. Läuger, P. 1991. The electrogenic ion pumps. Sinauer Publishers, Sunderland, MA.
33. Adam, G., P. Läuger, and G. Stark. 1988. Physikalische Chemie und Biophysik. 2nd Ed. Springer-Verlag, Berlin.