Stämpfli R. A new method for measuring membrane potentials with external electrodes. *Experientia* 10:508-9, 1954.
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This was the first publication of the newly invented "sucrose gap" method, which allows a short stretch of nerve or muscle fibre to be irrigated by an isotonic sucrose solution of high specific resistance. The external longitudinal resistance can grow to a multiple of the core resistance, so that membrane potential differences between the excitable membranes on either side of the gap can be measured at almost their absolute value. [The *SCI*® indicates that this paper has been cited in over 290 publications since 1955.]

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This short publication of a method owes its numerous citations to the fact that it contains an absolutely new idea. During my three autumnal stays of three months each at the ends of 1947, 1948, and 1949 in Cambridge with Alan Hodgkin and Andrew Huxley, I became more aware that currents that flow along nerve fibres can best be measured if a high resistance gap is produced either by pulling the preparation through a hole or through paraffin oil, thus reducing the volume of the external conducting medium. Huxley and I published a method to measure the absolute value of resting and action potentials of a single node of Ranvier by reducing the longitudinal current to zero by an electromotive force applied to the same external circuit. Such gaps, however, never have a high enough resistance to measure nearly 100 percent of the membrane potential, which should be possible if the external longitudinal resistance exceeds the internal one by more than 10-fold. The surface of the preparation always remains covered with a film of conducting solution and gains ions through the surface membranes.

After my return to Switzerland, I had difficulties in using the sophisticated methods to determine membrane potentials and decided to try a new way of obtaining a high external resistance. If an ion-free isotonic sucrose solution flowed along a bundle of nerve or muscle fibres in a gap, ions would be continuously removed and the resistance would become much higher than in ordinary paraffin oil or even air gaps. Such a sucrose gap (as I named it), when using isotonic KCl-Ringers with a bundle of myelinated nerve fibres, could measure about 90 percent or more of the nodal membrane potential value published by Huxley and me. I wrote a short paper and asked Huxley for critical comments. He sent a handwritten letter of 12 pages, 7 of them with calculations to estimate the errors caused by nonuniformity of the resistances and by junction potentials. To his surprise the errors were smaller than expected. His conclusion was: "In the end I quite expect that the errors are trivial and that it is all fuss about nothing. If the errors aren't bad—say only a few mV—the method is extremely useful and convenient."[1]

Most people who have used it since then, with all kinds of excitable tissues of adequate dimensions, seem to agree with him. Edith Bülbring, discouraged by intracellular measurements in smooth muscle, had wanted to abandon electrophysiology until G. Burnstock brought the sucrose gap method to Oxford. He had it from R.W. Straub, who was my first pupil in Homburg to use it in his thesis.[2,3] This earned me the compliment of having saved her from giving up. The theoretical problems contained in Huxley's letter have been treated by many colleagues.[4-8] One of them, John W. Moore, when I visited him, presented me to the audience as "sugar daddy," which may not have been so complimentary. Among many other more or less successful attempts to improve the method is one by C.H.V. Hoyle,[9] where some more citations may be found. My conclusion after so many years in the patch clamp era is that there is, particularly in pharmacology, a need for simple methods to measure membrane potentials and that my original idea is still useful. An improved version of the gap (among many others) is cited in reference 9.

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3. **Bülbring E & Burnstock G.** Membrane potential changes associated with tachyphylaxis and potentiation of the response to stimulating drugs in smooth muscle. *Brit. J. Pharmacol.* 15:611-24, 1960. (Cited 125 times.)
4. **Pooler J P & Valenzeno D P.** Reexamination of the double sucrose gap technique for the study of lobster giant axons. Theory and experiments. *Biophysical J.* 44:261-9, 1983.
5. **Lammel E.** A theoretical study on the sucrose gap technique as applied to multicellular muscle preparations. I. Saline-sucrose interdiffusion. *Biophysical J.* 36:533-53, 1981.
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7. ———. A theoretical study on the sucrose gap technique as applied to multicellular muscle preparations. III. Methodical errors in the determination of inward currents. *Biophysical J.* 42:159-70, 1983.
8. **Moore J W.** Comparison of voltage clamp with microelectrodes and sucrose gap techniques. (Smith T G, Lecar H, Redman S J & Gage P W, eds.) *Voltage and patch clamping with microelectrodes.* Bethesda, MD: American Physiological Society, 1985. p. 217-30.
9. **Hoyle C H V.** A modified single sucrose gap. Junction potentials and electrotonic potentials in gastrointestinal smooth muscles. *J. Pharmacol. Methods* 18:219-26, 1987.

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