

Weibel E R. Stereological principles for morphometry in electron microscopic cytology. *Int. Rev. Cytol.* 26:235-302, 1969.  
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In this review article, emphasis is placed on the possibilities of applying morphometric methods to correlative cell biology. The stereological methods useful in morphometric cytology are reviewed. Sampling strategies, statistical treatment, and choice of method are discussed by evaluating specific examples [The SCI® indicates that this paper has been cited in over 1,230 publications, making it the most-cited paper ever published in this journal].

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The work that led to this article started in 1959, when I joined the Cardiopulmonary Laboratory at Bellevue Hospital in New York, directed by the Nobel Laureates André Courmand and Dickinson Richards, who had done the pioneering work on cardiac catheterization. The laboratory was directed toward clinical and basic physiology, but I was hired as a morphologist "to do anything on the structure of the lung that is of interest to physiologists." Together with the Cuban biomathematician (and refugee) Domingo M. Gomez, who had then just joined the laboratory, we soon decided that lung structure could become "physiologically interesting" if it were reduced to numbers in a meaningful way. We developed the concept of what we began to call "morphometry" and applied it to the human lung.<sup>1</sup> After having spent two years with George E. Palade at Rockefeller Institute, I felt that the methods we had developed or adapted from other fields, such as metallurgy, should be particularly rewarding when used in cell biology to estimate cell composition or membrane areas on electron micrographs. The further development of these methods was to be greatly accelerated by the founding in 1963 of the International Society

for Stereology by Hans Elias, whom I succeeded as president for 1967-1971.

Besides continuing my research on structure-function relations in the lung, I engaged, after my return to Switzerland in 1963, in systematic morphometric studies on liver cells and their changes related to drug metabolism. The stereological methods used for this work needed to be perfected and made practical; on these methodological developments, done partly in close association with mathematicians, I have published many reports up to recent years, notably a two-volume book.<sup>2</sup> These methods have proved rather useful in our work as well as for other authors, and they have brought me an honorary fellowship in the Royal Microscopical Society. I have been made a foreign associate of the US National Academy of Sciences and have received the Marcel-Benoist Prize from the Swiss Government because of the "interest for physiologists" of these methods.

I was pleased to note that some of these methodological papers were frequently quoted, such as the paper in question and a paper published in 1966 in the *Journal of Cell Biology*.<sup>3</sup> The original 1966 paper had reported on newly developed methods to be used to quantify structural components of cells and tissues in electron micrographs. This paper probably received broad attention because it presented practical methods, based on a reasonably solid theoretical background, that researchers in an expanding field could use for many applications. It was not my only publication on the topic, but it was the one published in a prestigious journal, which lent it some special credibility! In 1969 I reviewed these methods, again with their practical application in mind. But I also added more on their theoretical background and expanded the practical side by working through specific examples from the choice of the method to sampling strategies and statistical treatment. However, I do not believe that the 1969 review brought much new progress, except for refinement.

I therefore find it somehow surprising that, as late as 1974, the 1969 review should have been more cited than the original 1966 paper. In the intervening years, I had, in fact, written a number of original papers dealing with improvements in particular aspects of stereological methods, and in 1979 I published a book on these methods,<sup>2</sup> but the 1969 paper still retains its prestigious position. I don't know why. Maybe it was particularly well written or it has become a habit to quote it and to be content with a "generally accepted" reference.

1. Weibel E R & Gomez D M. Architecture of the human lung. *Science* 137:577-85, 1962. (Cited 80 times)
2. Weibel E R. *Stereological methods*. London: Academic Press, 1979-1980. 2 vols
3. Weibel E R, Kistler G S & Scherle W F. Practical stereological methods for morphometric cytology. *J. Cell Biol.* 30:23-8, 1966 (Cited 970 times)