

Caro L G & van Tubergen R P. High-resolution autoradiography. 1. Methods. *J. Cell Biol.* **15**: 173-88, 1962.

The authors describe methods used in obtaining high resolution in autoradiography, with special emphasis on the technique of electron microscopic autoradiography, together with control experiments designed to establish the optimum conditions or procedures. These methods give a good localization of the label, at the subcellular level, and good reproducibility in relative grain counts. [The *SCI*[®] indicates that this paper was cited 637 times in the period 1962-1976.]

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This paper, together with its companion paper, ¹ described techniques for autoradiography of thin sections in the electron microscope and control experiments designed to establish the optimum conditions and procedures.

"While we were graduate students in biophysics at Yale University, Bob van Tubergen and I often tried to devise ways of improving resolution in autoradiography. We had discussed a number of times the possibility of using the electron microscope but had dismissed, on theoretical grounds, the notion that it might result in improved resolution. After our separate first attempts had clearly shown a very high level of resolution we, of course, revised the theory.

"In 1960 I was a post-doctoral fellow in the laboratory of Prof. George Palade, at Rockefeller University, and engaged, in collaboration with him, in a study on the role of the Golgi complex in protein se-

cretion. Bob van Tubergen's first results convinced me that electron microscopic autoradiography would be the best method for this study and I set out to develop techniques suitable for the study of thin sections. Soon after that, Bob was brought back from Europe, where he was spending his post-doctoral period, by an illness that would eventually interrupt a most promising scientific career. He then came to Prof. Palade's laboratory and, together, we developed the techniques described in this paper....

"I believe that the reason for the frequent citation of our paper is that it demonstrated clearly that high resolution autoradiography was possible without a drastic deterioration of the cytological structures in ultra thin sections. It also gave a set of simple recipes for the method. In my opinion, the main technical contribution was the introduction of the Ilford emulsion L4 to electron microscope autoradiography. Sixteen years later, and in spite of many attempts at finding a better product, it remains the most frequently used emulsion for this kind of work. Finally, I think the paper came at a time when electron microscope cytology was coming to the end of its purely descriptive phase and when cytologists were searching for experimental methods capable of giving indications as to the functions of the various intracellular organelles. Autoradiography provided one such method; hence the success of the paper.

"I would like to conclude these rambling notes by paying tribute to Bob van Tubergen who, while most of his energy was consumed in fighting, with admirable courage, a crippling disease, contributed so much, by his physical insight and his rigorous analytical mind, to the success of this work and of later experiments that utilized these techniques."

1. Caro L G. High resolution autoradiography. 2. The problem of resolution. *J. Cell Biol.* **15**:189-99, 1962.