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This Week's CitationClassic

Moor H & Mühlethaler K. Fine structure in frozen-etched yeast cells.
J. Cell Biol. **17**:609-28, 1963.
[Laboratory of Electron Microscopy, Department of General Botany, Swiss Federal Institute of Technology, Zurich, Switzerland]

The freeze-etch technique involves cleaving a frozen specimen and 'etching' it by vacuum sublimation. The fine structure of the etched fracture face is preserved in a replica obtained by condensing evaporated platinum and carbon onto it. The application of this replica technique to yeast cells showed for the first time that the problems of freezing artifacts can be overcome and that freeze-fractured membranes exhibit many structural details which are not portrayed by other techniques. [The *SCI*® indicates that this paper has been cited over 945 times since 1963.]

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"My interest in biology was first awakened by an uncle who is a plant ecologist, but hay fever blocked my way along this line; instead I decided to become a laboratory biologist. During my studies at the Swiss Federal Institute of Technology in the mid-1950s my enthusiasm for very small things was evoked by my teachers and later sponsors, A. Frey-Wyssling and K. Mühlethaler. In 1956 it was still an enormous challenge to enter the new and largely unexplored realm of cellular ultrastructure. In retrospect I can see that it was essential for my future work that from the beginning I became concerned with the problems of recognising and avoiding artifacts introduced by the preparation techniques used for electron microscopy. In those days freezing was suggested as being capable of solving the problems which arose from chemical fixation, embedding, and thin-sectioning. From the disappointing experiences of a colleague I learned that freeze-drying could not lead to success. But in 1957, a technique was published by Russell Steere which had all the features of **a** real alternative.[1]

"In the early 1950s several physicists had already used freezing in order to stabilize suspensions of diverse objects and, after cleaving the ice in order to disclose the inclusions, they produced a surface replica on the fracture face by condensing evaporated platinum and carbon onto it. The great merit of Steere was to have adapted this purely physical method for the preparation of biological objects. The pictures he published in 1957 showed well-preserved virus crystals in destroyed plant cells. These results and subsequent personal communications with him convinced me of the potentialities of the method and gave me insight into its technical limitations at that time. From this basis, I started the methodological development, a job which has kept me busy till now.[2]

"The work has proceeded along four different lines: development of an apparatus enabling fracturing, etching by vacuum sublimation of superficial ice, and coating of the frozen-fractured and etched specimen under high vacuum; precise physical control of every preparational step; freezing of cells and tissues without introducing artifacts due to ice crystal formation; and interpretation of the pictures which have given a completely new insight into cellular ultrastructure. A first breakthrough was the construction of a 'rather sophisticated' machine. Without the help of a bright technician, Heinz Waldner, and the commercial interest of a vacuum firm, this apparatus would never have been constructed and made generally available on the market.[3] The successful application of the technique to the investigation of yeast cell ultrastructure was published in 1963. It was evidently this second breakthrough which caught the attention of many scientists and —to judge from the large number of citations —was instrumental in the acceptance of freeze-etching as a standard preparation technique."

1. **Steere R L**. Electron microscopy of structural detail in frozen biological specimens.
J. Biophys. Biochem. Cytol. **3**:45-60, 1957.
[Citation Classic. *Current Contents (*47):17, 20 November 1978.]
2. **Moor H.** Recent progress in the freeze-etching technique. *Phil. Trans. Roy. Soc. London B* **261**:121-41, 1971.
3. **Moor H, Mühlethaler K, Waldner H & Frey-Wyssling A.** A new freezing-ultramicrotome.
J. Biophys. Biochem. Cytol. **10**:1-13, 1961.