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Behnke O & Forer -V. Evidence for lour classes of microtubules in individual cells. *J. Cell Sci.* **2**:169-42. 1967. [Dept. Anatomy, Royal Dental Coll.. and Carlsberg Foundation Biological Inst. Copenhagen. Denmark]

This paper cesenbes now microtudules in individual cells respond differently to the same treatments. From this it was argued that there are different classes, with different chemical and/or physical properties. [The *SCI*® indicates that this paper has been cited in more than 345 publications.]

Microtubules Are Not All the Same

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We met in Copenhagen in 1965. Olav Behnke had left his position as a surgeon to work towards his medical degree at the Royal Dental College. Arthur Forer had recently arrived, as an American Cancer Society postdoctoral fellow, at the Carlsberg Biological Institute, to work on *Tetrahymena* with Erik Zeuthen. Forer had worked on spindles in crane fly spermatocytes, using light microscopy,[1] and when Forer wrote Behnke for a reprint of a recent paper on electron microscopy of vertebrate cell microtubules[2] (microtubules being recently identified components of spindles), Forer suggested they meet to discuss mutual interests.

After meeting, we began work together on microtubules in various organisms. All the experimental work was done in the Dental College, a short bicycle trip from the Carlsberg laboratories. The collaboration was very fruitful—each of us contributed in different ways, one of those rare collaborations in which the total is more than just the sum of the parts. Forer did some solo work with *Tetrahymena,* but mostly we worked together. Of our resultant publications, the one that has been cited most is this *Classic* article. Up until that time, there was much descriptive work on microtubules in cells, but not much experimental work. One of the reasons this paper attracted attention was because it was one of the first to study microtubules experimentally, albeit inside the cell.

Another reason that this article attracted attention was because the results were heretical. Based on the descriptive work, most believed that all microtubules had identical properties. We treated whole cells, lysed cells, and sections; and we argued that, because different microtubules in the same cells responded differently to the same treatment, we could distinguish at least four classes of microtubules in individual cells. By this we meant that, though all microtubules appear the same in the electron microscope, they are not all the same; there are "intrinsic physical and/or chemical differences among the tubules themselves" in the different classes. We know now, many years later, that different microtubules can differ chemically: in addition to there being various tubulin genes (tubulin is the monomer protein that polymerizes to form microtubules), post-translational modifications produce chemically different microtubules.[3] Microtubuie behavior also depends on whether microtubules are associated with various proteins.[4]

We also reported on differences in response along the lengths of the 9+2 flagellar microtubules—i.e., not only were there differences among microtubules, but individual microtubules were different at positions along their lengths. This, too, recently has been confirmed.[5]

Our experiments 25 years ago were relatively crude compared to present experiments. Now, one can isolate components from cells and, with biochemical and genetic manipulation, study these components with relative ease. It is important to recognize that one studies components in vitro in order to understand how cells function, and that one must always ask whether and how the results from in vitro experiments relate to the cell. In our experiments with cells 25 years ago, the cells "told us" that the various microtubules differed among themselves and along their lengths: Only later did our colleagues learn how to study these differences in vitro. Our research interests have diverged somewhat, but we each continue to work with cells, and to try to have the cells reveal to us how they work.

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3. **MacRae T H & Langdon C N.** Tubulin synthesis, structure, and function: what are the relationships? *Biochem. Cell Biol.* **67**:770-90. 1989.
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