

## Citation Classics

**Lowry O H, Rosebrough N J, Farr A L & Randall R J.** Protein measurement with the Folin phenol reagent. *J. Biol. Chem.* **193**:265, 1951.

...The authors assert that the use of the Folin phenol reagent for the measurement of proteins "has not found great favor for general biochemical purposes." This study is concerned with modifying the Folin phenol reagent procedure by treating protein solutions "with copper in alkali." By recording the color change after the copper treatment, and measuring the quantity of protein present with a Beckman spectrophotometer, the authors determined that "measurement of protein with copper and the Folin reagent" is more sensitive and simpler than other procedures.

*Professor Oliver H. Lowry:*

... "It is flattering to be 'most cited author,' but I am afraid it does not signify great scientific accomplishment. The truth is that I have written a fair number of methods papers, or at least papers with new methods included. Although method development is usually a pretty pedestrian affair, others doing more creative work have to use methods and feel constrained to give credit for same<sup>1</sup>.... Nevertheless, although I really know it is not a great paper (I am much better pleased with a lot of others from our lab), I secretly get a kick out of the response....

"Perhaps you would be interested in a little about the history of the method. Back in 1922, Wu, who worked with Folin, applied the reagent to proteins, without  $\text{Cu}^{2+}$ , so it was based on the tyrosine and tryptophane contents of the protein. This procedure was used sporadically for some time and had a reputation for erratic results, probably because traces of contaminating  $\text{Cu}^{2+}$  would increase the readings. Herriot, in a 1935 footnote to another paper, mentioned that  $\text{Cu}^{2+}$  enhanced readings with protein, and in 1941 published a short communication describing the  $\text{Cu}^{2+}$  enhancing effect for 7 proteins, and giving convincing evidence that the enhancement was attributable to reaction with peptide bonds.

"Before I came to St. Louis we had need of a micro method for protein, studied the

reaction some more, and came up with a revised procedure which we felt was an improvement, particularly in regard to application to a variety of situations. Actually, however, we had made few fundamental changes from the method of Herriot, and had never really intended to publish it.

"When I came to St. Louis in 1947 Earl Sutherland, who was here then, adopted our procedure, but for several years complained that he had to cite it as 'personal communication,' and, he inquired, why didn't we write it up? So we finally went to work and did the necessary things: studied the reaction more thoroughly, tested it a lot of ways, described its virtues and disadvantages, compared the results with a Kjeldahl procedure, investigated what interfered, etc.

"This was a lot of work and the three co-authors helped in various ways. The greatest help was from Miss Nira Rosebrough (now Mrs. Nira R. Roberts) who became one of the best technicians I have ever had. She left us in 1957, worked for awhile with Dr. Rosen in Buffalo, and then quit science to raise a family. Dr. A. Lewis Farr (M.D.) was a post-doctoral student who had an outstanding record in medical school but decided after a year or so to go into private practice in his hometown in Greenville, Mississippi. Mrs. Randall was a technician who stayed at most a year, then left with her husband, and I don't believe has been in science since, but I have lost track of her.

"I...am puzzled why the paper is so often cited, and cited as such. I would like to think it is partly because we studied it pretty thoroughly and it is still applicable in most cases without modification, whereas the original Kjeldahl method, for example, has had innumerable major modifications and microfications, and people cite the particular modification they use. Another reason why our method isn't simply referred to by name is that it's quite a mouthful to say 'Lowry, Rosebrough, Farr, and Randall.' The method apparently filled a need in the beginning—and a lot of people measure proteins in their work. Once it became established by people like Sutherland and Kornberg, other people may have thought it was the method to use, or at least checked the procedure they were using against it."<sup>2</sup>

1. **Lowry O H.** Personal communication to D.J.D. Price, November 11, 1969.
2. **Lowry O H.** Personal communication to E. Garfield, August 5, 1976.