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Citation Classics

Nelson N. A photometric adaptation of the Somogyi method for the determination of glucose. *J. Biol. Chem.* 153: 375-80, 1944.

...The author reports a modification of the Somogyi method "for glucose determination in biological material." Somogyi's "copper reagents" are adapted for "colorimetric use" by omitting "iodide and iodate in their preparation." The author developed "a new arsenomolybdate reagent" which, when used with "Somogyi's micro reagent," gives "satisfactory stability and reproducibility of color."

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"It is a thoroughly pleasant but surprising experience to have one's paper, especially a very early one, referred to as a "Citation Classic." Many things have happened since that was published and many papers preceded and followed it, but apparently none has served as broad a practical end.

"I have always regarded the effort reported in that paper as a bit of emergency "engineering" to solve a major, and another secondary problem. In 1938, '39 and'40, I was working with a very bright and prolific colleague, Arthur Mirsky, at the May Institute for Medical Research in Cincinnati; and another talented investigator, Samuel Rappaport, at the Cincinnati Children's Hospital Research Foundation; and, with a brother, Waldo E. Nelson, also at the Cincinnati Children's Hospital (and also obviously talented). Work with these three collaborators, in one way or another, involved measurements of reducing carbohydrates, especially glucose, in a variety of ways. Thus, there were many irons in the fire; glycogenase, the movement of glucose and glycogen storage, kidney threshold studies, the role of phosphate in carbohydrate metabolism, and the control of diabetic children.

"Somewhere along the line, perhaps about 1940, all refrigerators in all available institutes were jammed with specimens awaiting analysis with which our staff, even with weekend work, were unable to keep abreast. Obviously something needed to be done and that was to improve the efficiency of glucose analysis, without losing the advantages of the Somogyi procedure.

"I was ready to tackle the problem; I needed only the time. It was clear that almost certainly the approach would have to be photometric, but that existing color reagents were unsuitable in a number of regards. However, the range of possibilities was not all that large. So, over the next few week-ends, through a series of cross sectional trials, I systematically varied components, and composition and methods of preparation of candidate color reagents as to their suitability for the quantitative estimation of the reduced copper oxide. It turned out that I could get the properties I needed from an arsenomolybdate and was able to devise two quite reproducible ways of preparing the reagent. These produced stable color densities directly proportional to the cuprous oxide, which were reproducible and with an absorption peak at a predictable wave length. This procedure was readily transferrable to the basic reduction technique of Somogyi, wherein it replaced the reliable but tedious titration method; in this way it greatly accelerated the analysis. Within a few weeks our refrigerators, though not precisely empty, were clearly ready to receive more specimens....

"There was a secondary problem which had to do with an annoying error which we detected in bloods deproteinized by the Somogyi procedure. So, back to the weekend chores. Actually the problem was fairly simple once I had clearly defined the difficulty. The solution was to use a barium rather than sodium hydroxide to precipitate the zinc, with the advantage that a surplus could be used, assuring removal of zinc while the excess barium was precipitated, leaving no nasty post-filtration residues to foul up the reduction process. I did feet it important enough to speak directly to Dr Somogyi about this and went to St. Louis to meet with him It was a delightful visit: Dr. Somogyi had the predictable Hungarian charm. He agreed that he was troubled with the same problem and that he had developed a remedy which in principle was identical to mine. His procedure, though similar, was more convenient than mine, and with his permission I included it in this paper. "[1]

1. **Nelson N.** Personal communication, November 12, 1976.