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Uriel J. Méthode d'électrophorèse dans des gels d'acrylamide-agarose (Method of electrophoresis in polyacrylamide-agarose gels).

Bull. Soc. Chim. Biol. 48:969-82, 1966.

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This paper describes the preparation of acrylamide-agarose gels and their standardization and utilization in electrophoretic separation of macromolecules. When gels are prepared at constant agarose content and at acrylamide concentrations of 3 to 9 percent, it is possible to fractionate proteins within a wide range of molecular weights. [The *SCC*® indicates that this paper has been cited in over 310 publications, making it the most-cited article from this journal.]

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I first became interested in electrophoretic techniques at the end of the 1940s when, as a medical student in Zaragoza (Spain), I worked in the physiology laboratory using paper electrophoresis to study serum proteins. At that time, this simple, inexpensive method was one of the few available to students because of the poor financial situation of Spanish university laboratories after the Civil War.

Several years later, in 1953, I was accepted as a graduate student in the laboratory of "chimie microbienne" (microbial chemistry) created and directed by Pierre Grabar at the Institut Pasteur, Paris, where the method of immunoelectrophoresis had just been perfected.¹ While actively participating in its development and applications, I came to be familiar with gel electrophoresis and then with agarose.

There, in the years that followed, and later (beginning in 1962) at the Institut de Recherches Scientifiques sur le Cancer in Villejuif in collaboration with Statis Avrameas, we developed techniques for enzyme characterization following electrophoresis and immunoelectrophoresis in these gels. Mean-

while, I also became interested in polyacrylamide gel electrophoresis, which was described in 1959.²

Having acquired solid experience in these different techniques, the idea naturally came to me of combining the excellent resolving power of acrylamide gels with the good mechanical properties of agarose gels. The preparations of mixed acrylamide-agarose gels posed only a minor technical problem that I believe we solved in collaboration with Josette Berges in a simple, easily reproducible manner, by first inducing polymerization of acrylamide at a temperature higher than the gelification point of agarose and then lowering the temperature so that the agarose gelatinized between the acrylamide polymer links.³ By using this process, and by keeping intact the agarose concentration while varying that of the acrylamide, it is possible to prepare mixed gels of varying porosity, thus allowing electrophoretic resolution of polypeptides or polynucleotides over a wide range of molecular weights.

I must confess that I was somewhat surprised upon learning that an article published in French, in a periodical with a relatively modest circulation, has been cited so often. The method no doubt filled a specific need at that time and was also very simple to use, requiring no special or costly equipment. I nonetheless believe that the publication in English of an adaptation of our method to the separation of nucleic acids, by Peacock and Dingman,⁴ as well as that of a general review of electrophoresis in acrylamide-agarose and its applications, written by our group,⁵ has contributed to its renown. It is very likely that the method is much less used nowadays, although it is still referenced or described in recent reviews and books on the field.⁶

Over the past several years, we have witnessed a veritable revolution in techniques for resolution and isolation of macromolecules with the rise in analytical and preparative chromatographic methods. These are of course very costly, requiring sophisticated equipment, but they have the advantage of giving excellent performance in terms of speed, reproducibility, and profitability. Indeed, they bear little resemblance to the rather "primitive" methods developed in past decades.

1. Grabar P & Williams C. Méthode permettant l'étude conjuguée des propriétés électrophorétiques et immuno-chimiques d'un mélange de protéines. Application au sérum sanguin. *Biochim. Biophys. Acta* 10:193-4, 1953. (Cited 1,820 times since 1955.)
2. Raymond S & Weintraub L. Acrylamide gels as a supporting medium for some electrophoresis. *Science* 130:711-13, 1959. (Cited 285 times.)
3. Uriel J & Berges J. Un nouveau support pour des séparations électrophorétiques: le gel mixte d'acrylamide-agarose. *C. R. Acad. Sci.* 262:164-7, 1966. (Cited 20 times.)
4. Peacock A C & Dingman C W. Molecular weight estimation and separation of ribonucleic acid by electrophoresis in agarose-acrylamide composite gels. *Biochemistry—USA* 7:668-74, 1968. [See also: Peacock A C. Citation Classic. *Current Contents/Life Sciences* 28(17):13, 29 April 1985.]
5. Uriel J & Berges J. Electrophoresis in polyacrylamide-agarose composite gels: an outline of the method in its applications. (Allen R C & Maurer H R, eds.) *Electrophoresis and isoelectric focusing in polyacrylamide gel*. Berlin: De Gruyter, 1974. p. 235-45.
6. Andrews A T, ed. *Electrophoresis: theory, techniques and biochemical and clinical applications*. Oxford: Clarendon, 1986. 452 p.