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Cleveland D W, Fischer S G, Kirschner M W & Laemmli U K. Peptide mapping by limited proteolysis in sodium dodecyl sulfate and analysis by gel electrophoresis. *J. Biol. Chem.* **252**:1102-6, 1977.

[Department of Biochemical Sciences, Princeton University, NJ]

This paper describes a rapid method for identification and characterization of proteins. The technique, which is especially suitable for analysis of proteins that have been isolated following electrophoresis in detergent-containing polyacrylamide gels, exploits partial enzymatic proteolysis and analysis of the cleavage products by gel electrophoresis. [The *SCI*® indicates that this paper has been cited in over 1,830 publications since 1977.]

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"As a result of its speed, resolving power, adaptability, and ease of use, polyacrylamide gel electrophoresis in the presence of the detergent sodium dodecyl sulfate is the most widely utilized method for the determination of both the purity and molecular mass of polypeptides in protein samples. This simple, but powerful, technique, first popularized by Weber and Osborn[1] and improved by Laemmli,[2] remains the centerpost of available methods for polypeptide analysis and characterization more than 16 years after its introduction.

"With the increased resolution of polyacrylamide gels, however, came a recurrent, companion problem: did polypeptides that shared indistinguishable mobility on such gels but were isolated using different methods or source materials represent biochemically related proteins or not? It was precisely this question that led to the initial attempt one Saturday morning to produce from a purified polypeptide a characteristic 'peptide map' of proteolytic fragments (now known as a Cleveland map). This was to be accomplished by intentional addition of a protease that would digest the substrate polypeptide, thereby leaving a series of cleavage products that could then be resolved using the previously mentioned, ubiquitous method of gel electrophoresis. Because of the difficulty in resolving very small peptide fragments, however, digestion conditions that produced large, stable fragments were required. This was achieved by the fortuitous but unexpected discovery that most commonly used proteases, which under normal conditions digest proteins into small fragments, yield large digestion products when the digestions are done in the presence of sodium dodecyl sulfate. From this observation, a very useful analytic technique (not to mention a 'classic' paper) was born.

"At that point, only the problem of publication remained. A manuscript was submitted to the *Journal of Biological Chemistry*, but to our amazement this was *rejected WITHOUT review* by an associate editor who inferred erroneously that a more comprehensive paper was to be sent elsewhere. Happily, when we inquired, we encountered the unusual situation of having the same editor instruct us that a resubmitted manuscript *without revision* would be accepted forthwith."

1. **Weber K & Osborn M.** The reliability of molecular weight determinations by dodecyl sulfate polyacrylamide gel electrophoresis. *J. Biol. Chem.* **244**:4406-12, 1969. (Cited 16,735 times.)
2. **Laemmli U K.** Cleavage of structural proteins during the assembly of the head of bacteriophage T4. *Nature* **227**:680-5, 1970. (Cited 23,635 times.)