

Edman P & Begg G. A protein sequenator. *Eur. J. Biochem.* 1:80-91, 1967.
[St. Vincent's School of Medical Research, Melbourne, Australia]

The protein sequenator is an instrument for the automatic determination of amino acid sequences in proteins and peptides. The degradation proceeds at a rate of 15.4 cycles in 24 hours with a yield in the individual cycle in excess of 98 percent requiring approximately 0.25 imoles of protein. [The SC][®] indicates that this paper has been cited in over 1,700 publications since 1967.]

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"In 1958, I joined St. Vincent's School of Medical Research as a junior laboratory assistant to Pehr Edman, who was developing his isothiocyanate method for protein sequencing.

"After observing the sequencing of proteins, I soon realised how repetitive it was. At a morning tea break one day, I suggested that a machine could be made to do this work, but because of my junior status, and the fact that the Edman degradation was a highly skilled technique, my comments met much derision from the other staff. About a week later, Edman (who, unknown to me, was also considering such a machine) took up the suggestion and after a day of intense discussion we had a clear idea of how a protein sequencing machine would work. We started with a simple glass chromatographic column, tilted, so that the protein would not simply fall out. Only a small part of the lower inclined surface would support the protein which certainly could be washed out. We realised that if the tilted column were rotated about its axis more of the inside

surface would be used, but the speed of rotation would have to be high so as not to form a simple spiral. At high speeds the protein would be held on the wall by centrifugal force but liquids entering at the top would not just pass down and out the tip but would rise up again when they reached the bottom. A vertical rotating column with a base would allow extracting liquids introduced to the bottom to rise up over protein on the wall and be scooped off at the top. Placed into a chamber that could be evacuated, we had the 'machine.'

"We first experimented with an old electric motor and a simple blown glass cup attached with sealing wax to the shaft. After a few hours we had the machine running and were satisfied that our initial ideas were feasible in theory and practice. Within 12 months (after building almost every piece three times), we had a prototype machine sequencing 34 amino acids in 53 hours.¹ Continually referring to the 'machine' soon became tiring so we affectionally named it 'Matilda' (Waltzing Matilda), but when it came time to publish, we renamed it 'sequenator.'

"We knew the sequenator had a much greater potential so we delayed publication of the complete paper for another three years until the performance was improved.

"The paper is highly cited because, until the invention of the sequenator, no single technique for sequencing was universally accepted. The sequenator immediately proved the isothiocyanate method as a procedure *par excellence* for sequencing proteins and peptides. We did not seek to patent the sequenator and the technology is freely available to all.

"Since publication, two significant developments^{2,3} have improved the performance and the introduction of the gas-phase sequenator⁴ could further advance protein sequencing. For a good overall review, see *Protein Sequence Determination*.⁵

1. Edman P. Determination of amino acid sequences in proteins. *Thromb. Diath. Haemorrhag.* (Suppl. 13):17-20, 1964.
2. Zimmerman C L, Appella E & Pisano J J. Rapid analysis of amino acid phenylthiohydantoin by high-performance liquid chromatography. *Anal. Biochem.* 77:569-73, 1977. (Cited 290 times.)
3. Tarr G E, Beccher J F, Bell M & McKean D J. Polyquaternary amines prevent peptide loss from sequenators. *Anal. Biochem.* 84:622-7, 1978. (Cited 240 times.)
4. Hewick R M, Hunkapiller M W, Hood L E & Dreyer W J. A gas-liquid solid phase peptide and protein sequenator. *J. Biol. Chem.* 256:7990-7, 1981.
5. Edman P & Henschen A. Sequence determination. (Needleman S B, ed.) *Protein sequence determination: a sourcebook of methods and techniques*. New York: Springer-Verlag, 1975. p. 211-79. (Cited 330 times.)