

Helenius A & Simons K. Solubilization of membranes by detergents.
Biochim. Biophys. Acta 415:29-79, 1975.
[Department of Serology and Bacteriology, Helsinki University, Finland]

This review paper describes the mechanisms of detergent action on biological and artificial membranes. The interactions between proteins and detergents are described in detail, and a conceptual framework is presented for the use of mild and denaturing detergents in membrane protein isolation and characterization. [The SCJ® indicates that this paper has been cited in over 1,235 publications since 1975.]

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April 17, 1985

This review article, centering on the actions of detergents on biological membranes, was an expanded version of the introductory chapter to my 1973 PhD thesis.¹ The background experimental work started several years earlier in Kai Simons's newly formed group in the Department of Serology and Bacteriology at the Meilahti Institutes for Theoretical Medicine. I joined Kai in 1967 as a second-year undergraduate student. Our daily contact continued in Finland and at the European Molecular Biology Laboratory in Heidelberg, until I moved to Yale in 1981. Kai served in the multiple roles of adviser, brother-in-law, friend, and collaborator. In the early days, we viewed ourselves as protein chemists, but our main interests were membranes and lipid-protein interactions.

At the time, the field of membrane biochemistry was in a state of confusion. The bilayer was just one of several models being considered, the dynamic structure of lipids was only starting to become apparent, and—most importantly for our work—the nature of membrane proteins and their interactions with lipids were poorly understood. Given their amphiphilic properties, membrane proteins were not soluble in aqueous solvents and thus not amenable to isolation for biochemical study.

This review paper, which Kai and I wrote during the rainy fall of 1974, combined our findings on detergent-membrane and detergent-membrane protein interactions with a general description of detergent properties, a summary of mixed deter-

gent-lipid systems, and a critical evaluation of previous results on membrane solubilization and reconstitution. It was a rather ambitious undertaking because we wanted to come up with a unifying theory for the observed phenomena of membrane solubilization and detergent binding to proteins.

Fortunately, we had access to a number of expert consultants both in Helsinki and abroad. The Meilahti Institutes, particularly the Department of Serology and Bacteriology, provided an exceptional environment for innovative and creative work. The department reflected the vision of its chairman, Olli Renkonen, who had brought together an active and enthusiastic team of young scientists, and who supported them with the full power of his authority. Across the hall from us was Ossi Renkonen, an excellent lipid and carbohydrate chemist, who was instrumental in demystifying for us the properties of lipids. Leevi Kaariainen, a dynamic virologist one floor up, introduced us to the Semliki Forest virus (an enveloped animal virus), which became our main model system. In addition, Henrik Garoff, Carl-Gustaf Gahmberg, Erkki Ruoslahti, Hans Soderlund, Carl-Henrik von Bonsdorff, Christian Ehnholm, and Jaakko Brotherus had great input in our work and our way of thinking. Working with this versatile group of researchers involved uninterrupted discussion about varied scientific topics and made up for many of the disadvantages of our relatively isolated location. One of the most important foreign "consultants" (available to us only through his published work and a brief encounter we once had in a crowded conference-center hall in Copenhagen) was Charles Tanford of Duke University. His work greatly aided our understanding of the thermodynamics of amphiphile interaction.

There are several reasons that the paper has been highly cited. The review was the first of its kind, it contained some crucial technical information about detergents in condensed form, and it apparently succeeded in explaining many of the conceptual problems that membrane researchers using detergents struggled with in their daily work. To our satisfaction, the unifying concept that we arrived at proved correct in its central features and has provided the basis for a large body of subsequent work in many laboratories. While still more difficult to handle than soluble proteins, membrane proteins no longer represent an insurmountable technical problem. Detergents allow solubilization of the membrane, replacement of protein-associated lipids, and reconstitution of proteins into artificial lipid bilayers.²⁻⁶

1. Helenius A. *The effects of detergents on membranes and lipoproteins*. PhD dissertation. Helsinki University, 1973.
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4. Lichtenberg D, Robson R I & Dennis E A. Solubilization of phospholipids by detergents. Structural and kinetic aspects. *Biochim. Biophys. Acta* 737:285-304, 1983.
5. Hjeltnelund L M & Chrambach A. Electrophoresis and electrofocusing in detergent containing media: a discussion of basic concepts. *Electrophoresis* 2:1-11, 1981.
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