

BOOK SERIES - 50th Year of Hacettepe University
Series Editor: Adil Denizli

CRYOGELS AND MONOLITHS

***Bo Mattiasson
Adil Denizli
Editors***



**HACETTEPE
UNIVERSITY
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Adil Denizli and Bo Mattiasson, Editors
Adil Denizli Series Editor

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PREFACE

We have proudly celebrated the 50th anniversary of the foundation of Hacettepe University. We take pride in being one of the most successful universities in Turkey and being ranked among the leading universities in the World. Since the year 1967, when Hacettepe earned the status of 'University', it has never given up on its principle of continuously going ahead and reaching for the very best. Hacettepe, always preserving its values and basic principles, has become a pioneer university that has been intertwined with the society and pursued innovations, achieving many "firsts" ahead of others.

From medicine to biology, philosophy, statistics, physics and chemistry; from history of arts to the English, German and French languages; from sociology to engineering, fine arts and conservatory, Hacettepe University started almost 50 years ago developing interdisciplinary collaborations across a wide range of scientific fields, a research trend which has achieved a status of global recognition in the 21st century.

Hacettepe University, which was recognized as "Research University" by the decision of Council of Higher Education, dated September 26, 2017, has built a strong "brand" image over these 50 years with its qualified and unique contributions to science in Turkey and has been the country's gateway to global scientific advances. It has graduated tens of thousands of students, each of whom has been our source of pride with their contributions to science, society and humanity as well as with their worldwide achievements. So have its graduates always been proud of Hacettepe.

Hacettepe University owes its success to its people who have always aimed to move forward by promoting interdisciplinarity and without giving up on the understanding "To the leading edge... Toward being the best..."

The Turkish and English series of books you are presented have been prepared in memory of the 50th anniversary of Hacettepe University by Prof. Dr. Adil Denizli, a distinguished researcher and faculty member who has heartily devoted himself to his university and science. Among the editors

and authors of the book series are respected scientists from Hacettepe University, Turkey and abroad. The series covers the studies from the multi-/interdisciplinary research areas of sciences, mainly from Medicine, Science and Engineering Sciences, which particularly stand out among the World's and Hacettepe's research interests.

Readers benefiting from these books will certainly appreciate the value of the profound contributions Hacettepe University made to science both in the country and in the World each time they see the name of "Hacettepe University" in the context of the authors, editors, footnotes, citations and bibliographies. This work is an expression of respect for Hacettepe University and for those who have meticulously served in this university for 50 years with an interdisciplinary understanding.

Thank you Adil Denizli... I would like to express my sincere gratitude and thanks to all those who have contributed to this precious work.

I wish many 50 more years to go forward in line with our motto "To the leading edge... Toward being the best..."

Prof. Dr. A. Haluk ÖZEN
Rector

PREFACE

In 1954 “Hacettepe” was founded in two chambers of an old Ankara house as a Chair of Child Health, then in 1967 officially earned “university” status. Hacettepe University celebrated its 50th anniversary in 2017 by proud of rich heritage and the positive, life-changing impact globally through the strength of our research, teaching, innovation and enterprise. In just 50 years Hacettepe University has managed to forge a powerful global reputation as a strong research-led university. To celebrate 50th anniversary numerous standout events were planned and performed by proud of past and dreaming of the future.

The Hacettepe Book Series are published to honor the five decades of work not only for the field but also for society at large and to leave the scientific mark of Hacettepe University to the history.

Adil Denizli, Ph.D
Editor

PREFACE

Separation of biomolecules has for long been more an art rather than a science. The development of chromatographic materials represented a quantum step where molecular sieving (sorting by size) was first introduced followed by ion exchange chromatography, affinity chromatography etc.. However, all these initial developments were dependent on use of chromatographic material with relatively small pores. That represented a severe limitation when it came to separation and isolation of large molecules and even particulate matter such as viral particles, bacterial cells, organelles and protein complexes.

Several efforts have been published to producing chromatographic media with macropores allowing separation of the objects listed above. One approach was characterized by that the polymerization took place while one was exploiting phase separation between the water phase with the monomers and an organic phase. Furthermore, some surfactants had to be added in order to facilitate the mixing of the phases, such that the polymerization took place in the space between the volumes of organic phase. After polymerization was completed, the organic solvent was washed out leaving behind a porous material that was evaluated for its chromatographic properties. Still, large pores (macropores) were difficult to produce. A common problem for all the efforts were a pronounced heterogeneity of the final product.

One alternative method to create chromatographic material with large pores was to aggregate small particles into small aggregates which were then aggregated into larger beads. Pores were left between the small aggregates. That system was attractive for immobilization of enzymes since mass transfer of substrate and products is facilitated.

With the introduction of cryogelation a new set of separation media could be produced. All the different modifications that had been reported for the conventional “old” separation media were now applied on the cryogels.

The strategy for producing the macroporous gels was to dissolve and mix the monomers in an aqueous solution which were supposed to build the polymers. Addition of catalytic system took place before the mixture was placed in a freezer. There ice crystals were formed from pure water while the dissolved compounds were excluded to the interstitial space between the network of ice crystals. After polymerization, the gels were thawed at room temperature, the water released when the ice melted and left behind a network of interconnected macropores big enough for housing cells and other particulate matter. The gels were named CRYOGELS since they had been produced by polymerisation in a cryo-environment. All different variations of liquid chromatography that earlier has been presented for conventional chromatographic matter has been applied on cryogels, with success. It was also demonstrated that composite gels could be produced by introducing different affinity particles thereby broadening the area of applications even further. Furthermore the new gels were also suitable for separating particulate material, a challenge that earlier was not possible.

When separating cells, it was also demonstrated that cells may very well be present within the cryogels and multiply there. This led into biomedical application of the gels.

This volume describes a range of different applications where cryogels are used both as tissue scaffold and as adsorbents in a range of different applications.

We are happy and thankful to the authors for their contributions which make up this volume.

Bo Mattiasson, Ph.D

Editor

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Bo Mattiasson started his research career as a PhD student at Lund University, with pioneering work on immobilized enzymes, multienzyme systems, and cells. During this time, he was under the supervision of Klaus Mosbach. After obtaining his doctoral degree in 1974, he was very rapid in starting an independent research group and was eventually appointed to a new chair in Biotechnology in 1985. He headed the Department of Biotechnology for 22 years until 2006, and during this period, the department has grown from a handful of people to more than 80 researchers and doctoral students. Over the years, Dr. Mattiasson has been the main supervisor of more than 60 doctoral students. The use of immobilization technology has permeated Professor Bo Mattiasson served as Biotechnology Advisor and Director of Bioprocess Control AB. Dr. Mattiasson has developed affinity techniques for bioseparation [6] that could be used early in downstream processing, such as affinity precipitation, in which the affinity ligands are coupled to the 'smart' polymers that undergo phase separation in response to changes in environmental conditions such as pH or temperature. During the past 10 years, he has been investigating the possibilities offered by macroporous cryogels for protein and cell separation and tissue engineering, and in wastewater treatment. He has written more than 500 papers in international journals, edited several books and has been on the editorial board of a handful of biotechnology-related journals.

Prof. Dr. Adil Denizli completed elementary and high schools in Ankara. He graduated from Chemical Engineering Department of Hacettepe University in 1985. He completed his MSc in 1986 with the studies on "Controlled Delivery of Anticancer Drugs from Polymeric Matrices". He got his Ph.D. degree with the thesis on "Specific Sorbents for Hemoperfusion" in 1992. He became an Associate Professor of Chemical Technologies in 1994. Dr. Denizli is the Hacettepe University Department of Chemistry Professor since 2000. Dr. Denizli has written over 500 articles and 5 invited review articles and 25 book chapters. He published 42 research articles in national journals and 100 popular science articles. He has 2 patents. He is one of the most cited scientists in chemistry and engineering field (18000 citations, over 2500 citations in handbooks, encyclopedias, books and thesis, h-index of 69). He served as an associated member of the Turkish Academy of Sciences from 1999 to 2007, and as a full member since 2007. Dr. Denizli has received "TUBITAK Encouragement Award" in 1998 for his studies on "Biomedicine, Biotechnology and Environmental Applications of Polymeric Matrices". He also received TUBITAK Science Award and Basic Science Award of Popular Science Magazine in 2006. He elected as the most publishing scientist of Hacettepe University between 1995-2005 by COMSTECH. He is an editor of the Protein Chromatography and New Generation Polymeric Systems book (Pozitif Press, 2010) and Affinity-Based Biosensors I and II (Kukla Press, 2015-2016) books, translation editor of Stryer's Biochemistry (Palme Press, 2014) and Principles of Chemistry: A Molecular Approach (Nobel Press, 2015) books. He is the writer of Bioseparation and Polymeric Carriers book (Turkish Academy of Sciences Press, 2011). He is an Editorial Board Member of 25 journals (Honorary Editor: Current Analytical Chemistry and Associate Editor: Current Applied Polymer Science, Bentham Science Publishers). He has supervised 59 Master of Science and 45 PhD theses and 5 post Doctoral research up to now. He organized 18 Chromatography Congress and 12 Affinity Techniques congress, 5 Graduate Summer Schools and 4 Graduate Course. He is married to Dr. Fatma Denizli and has one child (Alp Denizli).