SHELL SEMINAR SERIES
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Solute Partitioning and Diffusion in Hydrogels: Fundamentals of Drug Delivery

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ABSTRACT Hydrogels are biocompatible and, therefore, extensively applied, for example, in pharmaceutics, biomedicine, tissue engineering, and artificial organ scaffolds. Hydrogels also have application in a wide variety of bioseparation and biosensing processes. We focus specifically on hydroxyethyl-methacrylate (HEMA) /methacrylic acid (MAA) copolymer gels used in soft contact lenses to deliver drugs and comfort/wetting agents to the eye. In all applications, it is important to understand how aqueous solutes of varying size, molecular weight, charge, hydrophobicity, and configuration partition into and out of hydrogels which themselves are of differing water content, crosslink density (i.e., mesh size), and matrix charge density. Two-photon confocal microscopy and back extraction with UV/Vis-absorption spectrophotometry quantify equilibrium partition and diffusion coefficients for prototypical drugs, polymers, polyelectrolytes, and proteins transporting in HEMA gels with varying MAA contents. To express deviation from ideal partitioning, we define an enhancement or exclusion factor which, in turn, is a product of individual enhancement factors for size exclusion, electrostatic interaction, and specific adsorption. To obtain the individual enhancement factors, we employ an extended Ogston mesh-size distribution, Donnan equilibrium, and Henry's law characterizing specific adsorption to the polymer chains. Gels mesh sizes are obtained from measured linear oscillatory rheology; solute sizes are determined from measured bulk restricted-cell diffusion coefficients. Enhancement factors for various solutes vary between 10^{-3} and 10^{2} depending on gel charge and mesh size, and on solute size, charge, and chemistry. Predicted enhancement factors are in excellent agreement with experiment using no adjustable parameters. From transient two-photon confocal-microscopy concentration profiles, and back-extraction histories with UV/Vis-absorption spectrophotometry, we measure the corresponding solute diffusivities in the gels. We invent large-pore effective medium (LPEM) theory to account for solute size, hydrodynamic drag, and distribution of mesh sizes available for transport in the polymer network. Again, using no adjustable parameters, diffusivities predicted from the proposed LPEM model demonstrate good agreement with experiment. Our efforts provide a first step towards a priori design of hydrogels for uptake and delivery of specific water-soluble species by altering gel mesh size, polymer chemistry, and polymer backbone charge.

BIO **Dr. Clayton Radke** received his B.S. degree in chemical engineering at the University of Washington in 1966 and his Ph.D. in 1971 at the University California under the mentorship of J. M. Prausnitz. He spent 18 months as an NSF Postdoctoral Fellow at the University of Bristol studying colloid chemistry under Professors Douglas Everett and Ron Ottewill. In 1973, he joined the chemical-engineering faculty at the Pennsylvania State University returning to the faculty at the University of California in 1976. He rose to full Professor in 1984 and was appointed Professor of Vision Science in 2003. Dr. Radke has held a number of visiting professorships including the Universite de Poitiers, University of Minnesota, Massachusetts Institute of Technology, Stanford University, and KAUST, and was Benjamin Maeker Distinguished Professor at the University of Bristol in 2007. He won the Proctor & Gamble Colloid Chemistry Award of the American Chemistry Society in 2003, the John Franklin Carl Award of the Society of Petroleum Engineering in 2011, the Chemstations Research Lectureship Award of the American Society for Engineering Education in 2013, the University of Washington Alumnus of the Year in 2015, and Ruben Medal of the International Society of Contact Lens Researchers in 2019, and the Pioneer Award in Improved Oil Production of the Society of Petroleum Engineering in 2020. He was elected to the National Academy of Engineering also in 2015. Dr. Radke has lectured at well over 100 university and industrial laboratories. His lectures are appreciated for clear presentation of new technical advances sparked by humor and illustrative anecdotes. He currently serves on the editorial boards of 4 technical journals, several company technical boards, and is Chair of the Board of Trustees of New College in the Graduate Theological Union at Berkeley. Dr. Radke's research focuses on interfacial and colloidal technologies where phenomena at phase boundaries influence overall behavior. His research is rigorous and quantitative, blending fundamental theory with experiment. He tackles important problems that have large impact on practical application in industry. He has published over 300 research monographs, one book, and three patents, and delivered over 800 technical papers. Dr. Radke is devoted to teaching. He served as department vice chair for undergraduate education over almost two decades. He won the physical sciences Donald Sterling Noyce Prize for Excellence in Teaching in 1993, the UCB campus Distinguished Teaching Award in 1994, the Faculty Award for Outstanding Mentorship of Graduate Student Instructor in 2018, and the department teaching award 9 times.

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