

SCIENTIFIC ACCOMPLISHMENTS—MICHAEL F. BROWN

Professor Brown is a leading authority on the use of solid-state NMR spectroscopy and related biophysical methods to study liquid crystals, membranes lipids, and membrane proteins. Together with Joachim Seelig, he developed the use of deuterium (^2H) NMR spectroscopy for measuring the order parameters of biomolecules, which has since become one of the mainstays of biophysics. He also developed the use of nuclear spin relaxation in biophysics for investigating molecular dynamics. Novel applications unveiled the emergence of membrane elasticity over nano- and mesoscopic length scales. Additional NMR methods were implemented to study the structural dynamics of membrane proteins.

Notably, Brown integrated these findings together with the results of time-resolved electronic and Fourier transform infrared spectroscopy into a new biomembrane model that supersedes the standard fluid-mosaic model found in textbooks. The flexible surface model (FSM) explains how lipid-protein interactions underlie the tightly regulated lipid compositions of cellular membranes. It illuminates how the energy landscapes of liquid-crystalline biomembranes are connected with cellular functions in terms of the anisotropic stress field of the bilayer—a concept called frustration.

(1) Brown was the first to develop a comprehensive theoretical basis of the nuclear spin relaxation of biomolecules in terms of motional mean-square amplitudes (order parameters) as well as rates of structural fluctuations. In the case of lipid bilayers, the new model relates the energy landscape of the molecular fluctuations to emergence of elastic properties on the mesoscale—and even the nanoscale—of the stochastic bilayer deformations. His experimental measurements of the magnetic field dependence of the NMR relaxation rates of liquid-crystalline bilayers have been seminal for validating molecular dynamics (MD) simulations of membranes.

(2) For membrane lipids, Brown pioneered the development of solid-state NMR methods (order parameter analysis, relaxation methods) for the first detailed studies of lipid structure, ordering, and dynamics. His original implementation of solid-state NMR relaxation methods led to seminal concepts of collective membrane phenomena that emerge over mesoscopic length scales. Moreover, he extended these concepts to illuminate the roles of polyunsaturated lipids in biological signaling at the membrane level.

(3) Brown was the first to firmly establish how membrane lipids govern the energetics of membrane proteins, and he developed a new biomembrane model. According to the flexible surface model (FSM) developed by Professor Brown, elastic deformation of the membrane bilayer is coupled to the conformational energetics of membrane proteins, including receptors and ion channels. Frustration of the intrinsic curvature of the bilayer is linked to allosteric regulation of membrane proteins that are implicated in key signaling or transport functions.

(4) Just recently, he established how local motions of bound cofactors initiate the activation of membrane receptors. Brown showed for the first time how light-induced changes in the local dynamics of the retinal ligand stimulate large-scale activating fluctuations of rhodopsin. He proposed and critically tested a multiscale mechanism, whereby retinal triggers collective helical fluctuations in the activated state. He introduced the new concept of a dynamically activated receptor (DAR) as described by an ensemble activation model (EAM). His work continues to illuminate how the properties of biomembranes underlie key cellular functions with potential implications for human medicine and drug discovery.