# PREFACE

"Anesthesia" is a reversible drug-induced state that most importantly (for the surgeon, at least!), causes an inability to generate a motor response to what would normally be painful stimuli. The general anesthetic state includes unconsciousness and amnesia. These features are considered to be produced in the central nervous system, and in fact, when absent (e.g., during normal "awake" function), they collectively define consciousness. Thus, the study of general anesthesia overlaps with the study of consciousness—probably the most enigmatic state that exists! It should not be surprising then, that the range of experimental and theoretical approaches to understanding the anesthetic state is very large. We have attempted to capture the scope, complexity, and significance of the many approaches to understanding the state of anesthesia in this two-volume set of *Methods in Enzymology*. This is, perhaps, an unusual collection for MIE, in that many of the approaches do not fit the term "enzymology," or for that matter, even chemistry or biochemistry. This second volume: *Chemical and Biochemical Approaches for the Study of Anesthetic Function Part B* details structural approaches (X-ray crystallography, NMR, X-ray interferometry) focused on both soluble and membrane-bound proteins, many incorporating anesthetics. Also included are biophysical approaches for probing anesthetic binding affinity and localization, which include fluorescence, isothermal titration calorimetry, and electron paramagnetic resonance (EPR) techniques, as well as methods for generating and manipulating model membrane systems. We conclude this volume with a description of several cutting-edge in vivo approaches for studying anesthetic function. Novel drug discovery efforts are increasingly guided by light-triggered optoanesthetic and optogenetic approaches. Methods for profiling neuronal activity in space and time monitor changes in calcium secondary messenger, genome, and proteome. And, finally, novel applications of electroencephalography, PET, and MRI are helping to establish the relevant in vivo sites of anesthetic action. We have sought out the recognized experts in each field, to provide a succinct account of what these approaches can contribute and how to employ them most effectively. With such a diverse and intense campaign, one might have thought the mechanism of anesthesia would have succumbed by now! But this could not be further from the truth; despite finding ever-increasing use in modern medicine, anesthesia remains almost as enigmatic as when it was discovered over

170 years ago. Through further deployment and refinement of these approaches, and many more to be developed, we may finally reveal the mechanisms underlying anesthesia, and eventually improve it.

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