Methods in ENZYMOLOGY

Volume 492

Biothermodynamics, Part D

Edited by

Michael L. Johnson

Jo M. Holt

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VOLUME FOUR HUNDRED AND NINETY-TWO

METHODS IN ENZYMOLOGY

Biothermodynamics, Part D

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PREFACE

This volume is the continuation in a series of *Methods in Enzymology* volumes, which promotes thermodynamics as an important tool for the study of biological systems.

One of many examples of biological thermodynamics is the cooperative binding of oxygen by hemoglobin. Cooperativity is inherently a thermodynamic phenomenon. Hemoglobin is the quintessential example of a ligand-binding protein. Most biochemistry textbooks explain that the hemoglobin tetramer exists in two structural states, a low-affinity structure without oxygen bound and a high-affinity structure with oxygen bound. This is the classic two-state allosteric model as presented by Monod, Wyman, and Changeux (1965, *J. Mol. Biol.*, **12**, 88–118) and extended by Ackers and Johnson (1981, *J. Mol. Biol.* **147**, 559–582). Unfortunately, this model tells us nothing about the specific molecular interactions that are altered by the binding of oxygen which forces the hemoglobin to shift to the alternative structural state. Thermodynamics provides the conceptual and mathematical framework, that is, a "logic tool," for the investigation of the specific molecular interactions, and the concomitant energetics, such as those that are altered by the binding of oxygen which forces the hemoglobin to shift to the alternative structural and/or association states.

Unfortunately, a large fraction of scientists have the impression that thermodynamic approaches are archaic, and, at best, ancillary to the central issues of biochemistry. One reason for this misconception is that thermodynamics is commonly either poorly or not at all taught in departments of chemistry, biochemistry, etc. Another reason for this narrow and insular perception is that thermodynamics is frequently equated with a single experimental technique (i.e., calorimetry). Sadly, thermodynamics has seldom been fused with developments in molecular biology, structural analysis, or computational chemistry. However, all these perceptions are far from accurate.

Nevertheless, branches of the U. S. government have twice acknowledged Josiah Williard Gibbs for his contributions to thermodynamics and thus indirectly acknowledged the importance of thermodynamics. The first

acknowledgment was the U.S. Navy with the USNS Josiah Williard Gibbs which was a ship of the line between 1958 and 1971. The second example was the U.S. Postal Service by including him as one of four great American scientists on a series of postage stamps that were issued in 2005. "The greatest thermodynamicist of them all" (John Fenn, 2002 Nobel Prize in Chemistry).

MICHAEL L. JOHNSON, JO HOLT AND GARY K. ACKERS

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