Biophysical Chemistry 159 (2011) 1–5

Contents lists available at ScienceDirect

Biophysical Chemistry

journal homepage: http://www.elsevier.com/locate/biophyschem

Editorial

# Introduction: Twenty five years of the Gibbs Conference on Biothermodynamics

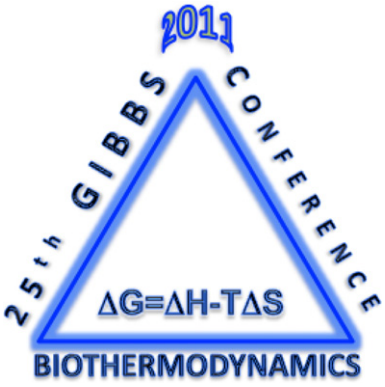
Madeline A. Shea [a,*], John J. Correia [b], Michael D. Brenowitz [c]

[a] Department of Biochemistry, Roy J. and Lucille A. Carver College of Medicine University of Iowa, Iowa City, IA, 52242-1109, United States
[b] Department of Biochemistry, University of Mississippi Medical Center Jackson, MS, 39216, United States
[c] Department of Biochemistry, Albert Einstein College of Medicine Yeshiva University, Bronx, NY 10461, United States

## HIGHLIGHTS

- The Gibbs Conference on Biothermodynamics ('Gibbs') is celebrating its 25th year.
- At Gibbs, half of the talks are given by students and postdoctoral associates.
- Gibbs promotes principles/methods for dissecting the molecular logic of biological systems.
- Gibbs connects structure and energetics to probe fundamental forces in molecules and cells.
- Biothermodynamics is fundamental to human health, disease, evolution and environmental change.

## GRAPHICAL ABSTRACT




## ARTICLE INFO

*Article history:*
Received 5 July 2011
Accepted 5 July 2011
Available online 21 July 2011

## ABSTRACT

In 2011, the Gibbs Conference on Biothermodynamics will celebrate its 25th anniversary. Since the inaugural meeting in 1987, it has brought together laboratories that lived, breathed and argued about the molecular logic of macromolecular machines. The participants have a deep commitment to understanding the nature of physico-chemical forces that govern regulation of biological systems, and share a passion for applying linkage theory. The collective goal is to understand how ligand binding, subunit assembly and conformational change drive what we observe as physiological processes such as regulated transport, enzyme cascades, gene regulation, membrane permeability, viral infection, intracellular trafficking and folding of macromolecules. In this special issue, articles by former organizers of the Gibbs Conference showcase the current breadth and depth of the field of biothermodynamics, and how thoroughly it is integrated with the study of macromolecular structures, computational modeling and physiological studies of human health and disease.



## 1. Introduction

In 2011, the Gibbs Conference on Biothermodynamics will celebrate its 25th anniversary. Since the inaugural meeting in 1987, it has brought together laboratories that lived, breathed and argued about the molecular logic of macromolecular machines. The participants have a deep commitment to understanding the nature of physico-chemical forces that govern regulation of biological systems, and share a passion for applying linkage theory (cf. [1–3]). The collective goal is to understand how ligand binding, subunit assembly and conformational change drive what we observe as physiological processes such as regulated transport, enzyme cascades, gene regulation, membrane permeability, viral infection, intracellular trafficking and folding of macromolecules.

The first meeting, called simply the *Biothermodynamics Conference*, included eleven research groups that convened at a rustic conference center associated with Southern Illinois University in Carbondale. It was centrally located, and very affordable. For the majority of participants,

* Corresponding author. Tel.: +1 319 335 7885; fax: +1 319 335 9570.
*E-mail address:* madeline-shea@uiowa.edu (M.A. Shea).

0301-4622/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.bpc.2011.07.002

the major cost was (and still is) transportation to the site. In 1989, the meeting was called the *Carbondale Conference on Functional Energetics*, and became the *Gibbs Conference on Biological Systems* in 1990. Soon thereafter, it became the *Gibbs Conference on Biothermodynamics*. For those who have grown up in the community of the meeting, it is referred to simply as "Gibbs", as in "What are you presenting at Gibbs this year?" The conference takes its name from Josiah Willard Gibbs whose concepts of free energy – the energy available to do chemical work – permeate our understanding of cellular processes.

The history of the first ten years was written by Gary K. Ackers and D. Wayne Bolen [4]. Over the course of that first decade, the format of the meeting evolved from a schedule in which one or two philosophical talks were given by faculty and the balance of research talks were presented by trainees, to its current format where about half of the talks are given by trainees and half by established independent investigators. Early in the evolution of the meeting, an evening scientific session on Saturday night was jettisoned in favor of a rousing welcoming reception as groups arrive from across the country – some having driven all day, and others making a shorter trip from the St. Louis airport. As the meeting grew from 44 participants in 1987 to almost 200 in recent years, more time to socialize and get acquainted was needed on the first night.

During daylight hours from early Sunday morning to Tuesday noon, the Gibbs Conference has five sessions of scientific talks, and afternoon workshops that focus on specialized interests. During the 24th Gibbs Conference, for example, Elisar Barber and Vince LiCata organized optional afternoon sessions for talks on education and public outreach. Several NSF CAREER awardees discussed their novel "broader impact" efforts. In other years, workshops have focused on scientific methods or data analysis.

Central to the success of the meeting has been its inclusion of students and post-doctoral researchers as presenters and colleagues, and its emphasis on teaching the principles, philosophy and methods underlying the research. Attendees at crowded poster sessions on Sunday and Monday night debate how fundamental properties of free energy, enthalpy and entropy are manifest in macromolecules. They argue over interpretations, models and methods. These vigorous discussions are followed by beachside campfires that sparkle with conversations that run long after midnight. Scientific collaborations and enduring friendships have been formed in this unstructured setting.

The ongoing strong emphasis on training is an essential element that distinguishes this conference from most others. The founders recognized that graduate students and postdoctoral fellows needed to become the next leaders in the field for the field itself to continue to be vibrant. This tradition has cultivated an inter-generational community of biothermodynamicists. Individuals who attended the conference first as students have connected with postdoctoral mentors and continued to attend. They now come to the meeting as principal investigators themselves with their own trainees. Those who attend the meeting are dedicated to participating in a collective training exercise, and willingly share their expertise. It is common to see small groups gather in the upper level of the dining hall during the evening poster session to crowd around a laptop and look at preliminary data together. In addition to the data clinics, it is common to have a demonstration of the newest "beta form" of software on an experimental problem of mutual interests. New collaborations have grown easily out of this casual environment in which the PI's are outnumbered by the trainees.

Related to data analysis and method development, we wish to call attention to the pivotal role that Mike Johnson has played in educating our community about the essential interplay between design and analysis of experimental studies, as well as the importance of evaluating asymmetric confidence intervals and conducting global analysis. In a series of Methods in Enzymology volumes edited with Gary Ackers and Jo Holt, and another with Lenny Brand, Mike has contributed to expanding current references for relevant techniques,

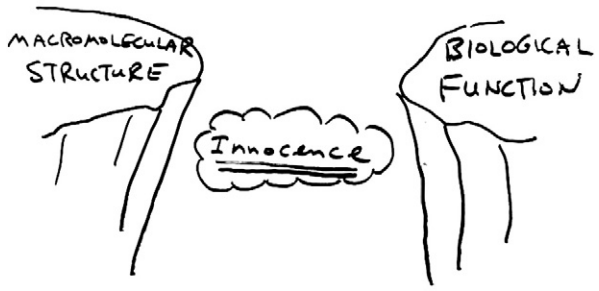



**Fig. 1.** Chasm between structure and function.

and his chapter written with Susan Frasier [5] remains one of the most readable accounts of methods for data analysis. Similarly, Jack Correia organized a volume in *Methods in Cell Biology*[6]) that highlighted biophysical approaches to understanding cellular phenomena and included contributions from many members of the Gibbs community.

Even in this day of Internet-assisted face-to-face discussion (e.g., Skype) or free dissemination of video presentations (e.g., YouTube), there is nothing that rivals the synergy created when strong-minded people with passionate views get together and discuss their ideas and approaches. When the Gibbs Conference began, few scientists had access to electronic mail consistently (Bitnet was available, but networks were modest and modems were used to access telephone lines). Now, scientists suffer from E-fatigue. The Gibbs Conference, or "Thermo Camp" as some of its enthusiasts refer to it, is a wonderful shot in the arm. Perhaps the simplest encapsulation of the Gibbs Conference is that it represents a home for "free energy" – where ideas central to chemical work are used without definition or apology. The founders envisioned the meeting as a forum for the continued development of thermodynamic theory and its application to an expanding series of biological questions. The success of the mission is reflected in the succession of present attendees and conference organizers.

## 2. In the beginning – 1987

In 1987, the deep chasm between structure and function could be summarized by Fig. 1, a diagram drawn by Gary Ackers and presented early in the life of the Gibbs Conference.

In many areas of biochemistry, the triumph of obtaining representations of proteins and DNA at atomic resolution led to unbridled structural euphoria that led to inferring mechanisms of protein function on the basis of a single (or a few) high resolution structures of endstate conformations. The events occurring between the first and final act of a process were envisioned as continuous adjustments (what we now call "morphs") of those endstates, and many creative scientists sought "the (single) pathway" to enlightenment of a mechanism in the same way that one might try to trace the propagation of transferred momentum through a "Rube Goldberg" machine. Never mind that energetics drives probability, and that we can rarely freeze intermediate states for observation. While it is natural and exciting to invent models for what we cannot see, some of these hypothetical mechanisms took on the mantle of verified truth. After all, they arose from exquisitely detailed data sets that were visually attractive (i.e., in color), and were starting to rotate in real time on the early graphics terminals of the 1980's (as Evans and Sutherland systems gave way to Silicon Graphics workstations and, then, ultimately to visualization and modeling software running on every desktop and laptop computer).

Devotion to rigor and clarity of thought have been preserved throughout the years, but the meeting has evolved to reflect our expanding capacity to probe and predict the behavior of larger and

more complex macromolecular assemblies. Furthermore, experimental studies have moved from being conducted almost exclusively *in vitro* to encompassing a broader range of *in situ* and *in vivo* studies [7].

An example of the evolution of the meeting is seen in the study of allostery. In the early years of the Gibbs Conference, talks about allostery were dominated by analyses utilizing the theory of linked functions developed by Wyman [3,8], Ackers free energy coupling [9] and comparison of the two classical models of allostery, Monod–Wyman–Changeux (MWC) [10] and Koshland–Némethy–Filmer (KNF) [11]. These are powerful approaches and even now, are not fully understood by many in the biomolecular community. However, as time has passed, conference talks now focus on direct interrogation of allosteric intermediates, structural correlations and the role played by dynamics and conformational fluctuations in mediating communication within macromolecules. Computational and structural biology methods, as approaches that illuminate dynamics, have become a solid thread in the tapestry of avenues of inquiry by biothermodynamics. No one blinks when we discuss the linkage between folding and binding, once viewed as separate and sequential processes.

The Gibbs community has worked to merge structural and energetic analysis. While thermodynamics had been viewed through the 1970's as providing global and precise but "low resolution" (i.e., non-mechanistic) information about free energy, enthalpy and entropy, in the 1980's experimental approaches including NMR [12,13], fluorescence [14], and chemical and enzymatic footprinting [15] were being validated to monitor individual residues, binding sites, domains or subunits while other approaches, including electrophoretic mobility shift analysis [16–18] and cryo-electrophoresis [19,20]) allowed us to monitor the abundance of individual species. These methods came close to being the Maxwell's Demons that would reveal the relative abundance of distinct states of a biological system. During this time, new theories were being developed to determine how cooperative free energy partitions between sites and domains.

Development of single-molecule and optical-trapping experiments now provide unparalleled opportunities to understand the behavior of individual molecules. But, in the end, the dances performed by these peripatetic travelers on cellular highways are still constrained by the laws of thermodynamics. So, we find that classical thermodynamics still has power as a logic tool to rule out mechanisms or provide boundary conditions for any molecular mechanism that can be visualized with ever increasing detail. This philosophy is summarized in Fig. 2, a diagram that Gary Ackers presented at the Gibbs Conference when discussing the future of the field and a philosophical approach to linking concepts and data.

### 2.1. A snapshot of current progress

The members of the Gibbs community have the deepest respect for the principle that "the same equations have the same solutions." Time spent understanding classical systems in deeper detail will pay off because the scientific community may apply those principles more rapidly to newly discovered partners in biological pathways. It has been humbling to recognize that thousands of person years of work across the globe have been devoted to determining the regulatory mechanisms of even well studied allosteric systems such as hemoglobin [21]. However, the lessons learned from these approaches, and particularly the importance of identifying the properties of intermediate states, have generated deep respect for the complexity of macromolecular switches.

Over the past 25 years, participants in the Gibbs Conference also have embraced new systems, new concepts and methodologies. This Special Issue of *Biophysical Chemistry* (edited by Enrico Di Cera, Jack Correia and Tim Lohman) features contributions from past organizers of the conference showcasing current research in biothermodynamics. The concepts and tools of this field serve as the basis for investigations of biological circuits in which we try to identify and connect the underlying populated states to the rules for transition in the system. This is equivalent to saying that we seek to understand what drives changes in the distribution of molecular states – it is not the same as asking for "the pathway". If site-directed mutagenesis has taught us anything, it is that many macromolecules have redundant pathways that are regulated by subsets of effector molecules. The biochemistry community completely underestimated this. When we moved from using protein from alternative species (e.g., myoglobin

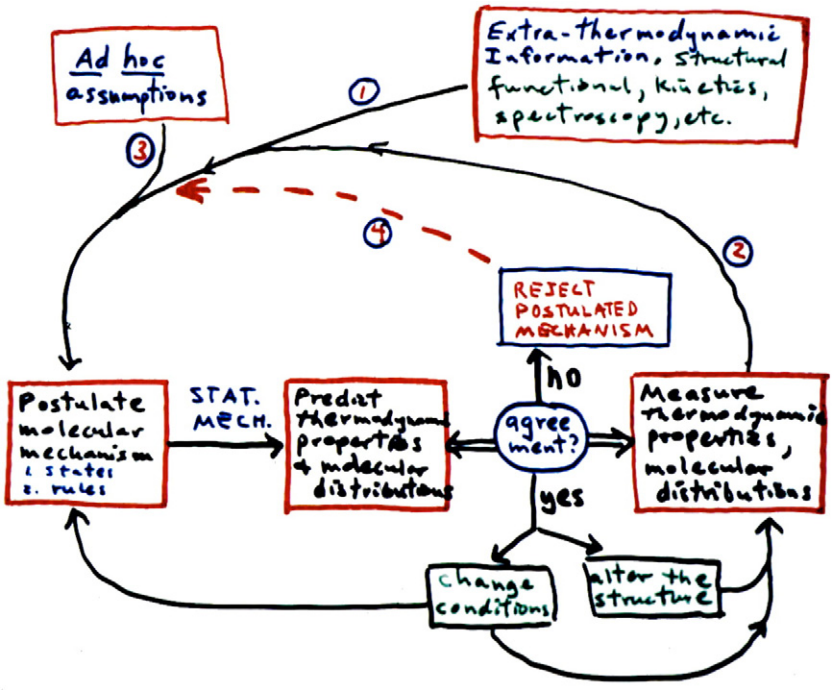



**Fig. 2.** Flowchart for Integrating Thermodynamic and Structural Experimental Data with Theory to Understand Molecular Mechanisms. All paths lead back to refining formulations of the states and rules (the hardware and software, or grand partition function) of the biological system. Data and insights are culled from many types of experiments to inform the development of predictive models of the interacting macromolecules and their allosteric effectors such as pH, or small molecular ligands. Figure drawn by Gary K. Ackers.

from a wide range of mammals) as our source of variations to making mutants in the lab, some investigators predicted the demise of protein research when "all the answers" would be easy to obtain. Little did we appreciate that proteins had so much more to teach us, and that it would be so difficult to design them a priori to have specific activities, much less be regulated. Determining the partition function requires a multi-faceted understanding of the concepts of thermodynamics, and kinetics as well as knowledge of multiple structures preferably determined using a combination of methods, including constraints from solution methods such as NMR and SAXS.

A network of intramolecular and intermolecular interactions can be simulated with a wide variety of computational methods. Although some calculations still require significant programming expertise, more opportunities are within the grasp of very junior students than ever before. University courses routinely use spreadsheet programs to simulate the behavior of a poly-protic acid, or binding of a repressor to a multi-site DNA operon. More sophisticated software such as *Mathematica* simplifies the preparation of clear and intuitive figures for sharing experimental results and making models used in academic courses and in research publications.

The revolution in molecular biology, genomics, screening methods and spectroscopy also has benefited the biothermodynamics community enormously, allowing theories about fundamental forces to be tested directly through manipulation of the chemical composition of molecules and cells. This is evident in contributions that probe thermodynamic principles governing protein regulation and design [**Garcia-Moreno** [24], **Barrick** [25]]. The goal of dissecting allosteric interactions within and between macromolecules has benefited from advances in experimental methods that probe site-specific interactions and from increases in computational power that permit realistic comparisons of microscopic distributions and macroscopic system properties [**Barbar** [26], **Clark** [27], **Hilser** [28], **Shea** [29]]. Some members of the community are now applying classical methods of analysis (such as analytical ultracentrifugation) directly to patient samples [**Correia** [30]].

Enormous advances have occurred in our understanding of the complexity of nucleic acid structures, and the enzymes that modify them. Several contributions in this issue focus on the folding and binding properties of DNA [**Marky** [31], **Chaires** [32]], and how proteins recognize RNA **[Hall** [33]] or DNA **[Bain** [34]**, Heyduk** [35], **LiCata** [36], **Lohman** [37]]. In 1987, many proteins were viewed as 2-state "on" or "off" switches; to some, it had seemed excessive to postulate 40 states of the bacteriophage lambda right operator and its control of the lysogenic-to-lytic growth switch [22]. However, in 2011, we are still expanding our understanding of the role of hinges and domains in protein-DNA interactions and gene regulation [**Beckett and Swint-Kruse** [38], **Lee** [39], **Sharp** [40]].

The concept of ligand-induced folding is now a textbook theme in biothermodynamics. Several contributions in this special issue probe how protein stability or conformational states are linked to binding small molecules or ions, and how these regulatory interactions influence proteins important to health and disease [**Brenowitz** [41], **Di Cera** [42], **Makhatadze** [43], **Pappu** [44]]. Cooperativity between folding units [**Fleming** [45], **Henzl** [46]] and a deepening understanding of how solutes in the cellular milieu contribute to protein stability [**Bolen** [47]] have taken us far from the 1987 arguments over whether and how many intermediates might be populated during the transition between "the" native and "the" unfolded state(s) of a protein.

Despite the enduring qualities of the Cantor and Schimmel text on Biophysical Chemistry (especially Volume 3 on the behavior of macromolecules [23]), we have moved from a time when textbooks are the primary source for graduate biophysical chemistry courses. We are now in a time when we turn first to the primary literature which is easily searchable online. We hope that the collection of articles in this issue may serve as the basis for a stimulating introduction to the field of biothermodynamics, conveying the excitement of its authors and the promise of its approaches.

### 2.2. Looking forward

The study of biothermodynamics is now rich in detail and nuanced with respect to the impact of measurements in areas ranging from human health and disease to environmental effects and a molecular understanding of the evolution of species. Investigators are increasingly committed to connecting new findings to relevant biological phenomena. Indeed, it is rare to hear a talk about thermodynamics that does not put the work into the perspective of known macromolcular structures and health or development of the biosphere. Conversely, life has existed in many forms on our planet. Whether to transduce energy from the sun, or mediate storage and transfer of energy between meals or seasons, whether acting at an undersea vent or in a classroom, the same laws of thermodynamics have put pressure on all of these biomolecules.

There are features of regulation that are only knowable by measuring the energetic contributions of ligand binding, assembly and conformational change. Regardless of how many structures are determined at high resolution or how much "high through-put screening" data is collected, making accurate connections between them, and determining their relative abundance in a cell, can only be done by understanding the forces that drive change (i.e., applying the tools of biothermodynamics). To fully conquer the chasm in Fig. 1, we must be dedicated to helping the broader scientific community understand that determining "the states and the rules" (i.e., discovering the functional energetics) is tantamount to revealing the software that is running the hardware, and that this work will yield mechanistic understanding.

To emphasize how concepts in molecular and cellular biophysics are linked, we chose to assemble the sessions of the 25th anniversary conference, according to ideas rather than systems. For example, the Keynote lecture will be presented by Bertrand Garcia-Moreno in a session called *Structural Origins of Thermodynamic Potentials.* In a later session on *Solvent and Solute Interactions with Macromolecules*, speakers will discuss how the chemical milieu affects macromolecular behavior by looking at salt effects on nucleic acids and proteins, osmolyte effects on proteins, and membrane effects on proteins (and vice versa). In the session *Thermostability and its Pressure on Evolution of Macromolecule*, we will hear talks on both RNA and proteins because they obey the same laws of thermodynamics in the same compartments of cells.

In considering how to recapture the intimate feel of those earlier (much smaller) meetings, and to help trainees self-assemble, we are introducing a new "trainee only" event on Saturday night. With Vince LiCata and Liskin Swint-Kruse as the faculty organizers, the trainees will have a private dinner, present flash talks, and pepper a panel of scientists in the private sector and academia with questions about where biothermodynamics has taken them in their careers. Then, they will join the meeting-wide reception to launch more connections.

### 2.3. Closing

Much as physics and chemistry moved from a Newtonian view to embrace the wave-particle duality of light, atomic orbitals and semiconductors, the molecular study of biology has moved from a phenomenological and descriptive field to one that understands that distributions of molecules are critically important, and that energetics drives those distributions. Whether we consider an ensemble of fluctuations experienced by a single molecule, or an ensemble of states for many molecules in a population, the probability of biological events depends on those distributions. Understanding what regulates the distributions and modeling what will happen when a regulatory molecule is mutated or responds to solutes, temperature or pressure is at the very core of biothermodynamics.

The future of this field is bright as it becomes ever easier to dissect how macromolecules operate and to demonstrate these principles by making intuitively accessible graphic representations of equations linking stability, binding and conformational change. We can reach across the globe and share expertise in video formats. But, we cannot relegate the dissemination of our field to passive activities on the world-wide web. There will continue to be a critical role for bringing the "Gibbs community" together at a small conference center and letting them shake, rattle and roll for a few days each fall.

Having the Gibbs Conference reach its 25th anniversary is due in large part to energetic efforts of the founders and their research groups. With deep sadness, the community never had the chance to enjoy having Stan Gill participate in the meeting that he helped create. His untimely passing left a void in the linkage community. But his colleagues have contributed to the meeting and the field. In the ensuing years, Gary Ackers, Wayne Bolen and Jim Lee were stalwart supporters of the Gibbs Conference. They patiently and enthusiastically advised attendees of the conference, including many outside their own laboratories, who were beginning to initiate independent careers. We look forward to talks by Jim and Wayne at the 25th Gibbs Conference, and regret that Gary Ackers passed away this May [48]. He will be with us in spirit.

## References


[1] J. Wyman, S.J. Gill, Binding and linkage: functional chemistry of biological macromolecules, University Science Books, Mill Valley, 1990.
[2] E. Di Cera, Thermodynamic theory of site-specific binding processes in biological macromolecules, Cambridge University Press, Cambridge, UK, 1995.
[3] J. Wyman Jr., Linked functions and reciprocal effects in hemoglobin: a second look, Adv. Protein Chem. 19 (1964) 223–286.
[4] G.K. Ackers, D.W. Bolen, The Gibbs conference on biothermodynamics: origins and evolution, Biophys. Chem. 64 (1997) 3–5.
[5] M.L. Johnson, S.G. Frasier, Nonlinear least-squares analysis, Methods Enzymol. 117 (1985) 301–342.
[6] J.J. Correia, I.H. William Detrich, Biophysical tools for biologists, in vitro techniques, in: J.J. Correia, I.H. William Detrich (Eds.), Methods in Cell Biology, Academic Press, 2008.
[7] J.J. Correia, I.H. William Detrich, Biophysical tools for biologists, in vivo techniques, 2009.
[8] J. Wyman, The binding potential, a neglected linkage concept, J. Mol. Biol. 11 (1965) 631–644.
[9] G.K. Ackers, M.A. Shea, F.R. Smith, Free energy coupling within macromolecules: the chemical work of ligand binding at the individual sites in cooperative systems, J. Mol. Biol. 170 (1983) 223–242.
[10] J. Monod, J. Wyman, J.-P. Changeux, On the nature of allosteric transitions: a plausible model, J. Mol. Biol. 12 (1965) 88–118.
[11] D.E. Koshland Jr., G. Némethy, D. Filmer, Comparison of experimental binding data and theoretical models in proteins containing subunits, Biochemistry 5 (1966) 365–385.
[12] I.M. Russu, N.T. Ho, C. Ho, A proton nuclear magnetic resonance investigation of histidyl residues in sickle hemoglobin, Biochemistry 21 (20) (1982) 5031–5043.
[13] H. Roder, G.A. Elove, S.W. Englander, Structural characterization of folding intermediates in cytochrome c by H-exchange labelling and proton NMR, Nature 335 (No.6192) (1988) 700–704.
[14] W. Bujalowski, T.M. Lohman, A general method of analysis of ligand-macromolecule equilibria using a spectroscopic signal from the ligand to monitor binding. Application to *Escherichia coli* single-strand binding protein-nucleic acid interactions, Biochemistry 26 (1987) 3099–3106.
[15] M. Brenowitz, D.F. Senear, M.A. Shea, G.K. Ackers, Quantitative DNase footprint titration: a method for studying protein–DNA interactions, Methods Enzymol. 130 (1986) 132–181.
[16] M. Fried, D.M. Crothers, Equilibria and kinetics of lac repressor-operator interactions by polyacrylamide gel electrophoresis, Nucleic Acids Res. 9 (#23) (1981) 6505–6525.
[17] M.M. Garner, A. Revzin, A gel electrophoresis method for quantifying the binding of proteins to specific DNA regions: application to components of the *Escherichia coli* lactose operon regulatory system, Nucleic Acids Res. 9 (13) (1981) 3047–3060.
[18] J. Carey, Gel retardation at low pH resolves TRP repressor-DNA complexes for quantitative study, Proc. Natl. Acad. Sci. U. S. A. 85 (1988) 975–979.
[19] M. Perrella, N. Davids, L. Rossi-Bernardi, The association reaction between hemoglobin and carbon monoxide as studied by the isolation of the intermediates. Implications on the mechanism of cooperativity, J. Biol. Chem. 267 (1992) 8744–8751.
[20] D.L. Bain, G.K. Ackers, A quantitative cryogenic gel-shift technique for analysis of protein-DNA binding, Anal. Biochem. 258 (1998) 240–245.
[21] G.K. Ackers, J.M. Holt, Asymmetric cooperativity in a symmetric tetramer: human hemoglobin, J. Biol. Chem. 281 (2006) 11441–11443.
[22] M.A. Shea, G.K. Ackers, The $O_R$ control system of bacteriophage lambda – a physical–chemical model for gene regulation, J. Mol. Biol. 181 (1985) 211–230.
[23] C.R. Cantor, P.R. Schimmel, Ligand interactions at equilibrium, Biophysical Chemistry Part III: The Behavior of Biological Macromolecules, H.W.Freeman and Co., New York, 1980, pp. 849–886.
[24] P. Bell-Upp, A.C. Robinson, S.T. Whitten, E.L. Wheeler, J. Lin, W.E. Stites, B. García-Moreno E, Thermodynamic principles for the engineering of pH-driven conformational switches and acid insensitive proteins, Biophys. Chem. 159 (2011) 217–226.
[25] E.F. Vieux, D. Barrick, Deletion of internal structured repeats increases the stability of a leucine-rich repeat protein, YopM, Biophys. Chem. 159 (2011) 152–161.
[26] A. Nyarko, J. Hall, A. Hall, M. Hare, J. Kremerskothen, E. Barbar, Conformational dynamics promote binding diversity of dynein light chain LC8, Biophys. Chem. 159 (2011) 41–47.
[27] J.L. Schipper, S.H. MacKenzie, A. Sharma, A.C. Clark, A bifunctional allosteric site in the dimer interface of procaspase-3, Biophys. Chem. 159 (2011) 100–109.
[28] J.O. Wrabl, J. Gu, T. Liu, T.P. Schrank, S.T. Whitten, V.J. Hilser, The role of protein conformational fluctuations in allostery, function, and evolution, Biophys. Chem. 159 (2011) 129–141.
[29] T.I.A. Evans, J.W. Hell, M.A. Shea, Thermodynamic linkage between calmodulin domains binding calcium and contiguous sites in the C-terminal tail of $Ca_V1.2$, Biophys. Chem. 159 (2011) 172–187.
[30] J.L. Cole, J.J. Correia, W.F. Stafford, The use of analytical sedimentation velocity to extract thermodynamic linkage, Biophys. Chem. 159 (2011) 120–128.
[31] S. Maiti, B. Kankia, I. Khutsishvili, L.A. Marky, Melting behavior and ligand binding of DNA intramolecular secondary structures, Biophys. Chem. 159 (2011) 162–171.
[32] R.D. Gray, J.B. Chaires, Linkage of cation binding and folding in human telomeric quadruplex DNA, Biophys. Chem. 159 (2011) 205–209.
[33] S.G. Williams, K.B. Hall, Human U2B″ protein binding to snRNA stemloops, Biophys. Chem. 159 (2011) 82–89.
[34] K.D. Connaghan, A.D. Moody, J.P. Robblee, J.R. Lambert, D.L. Bain, From steroid receptors to cytokines: The thermodynamics of self-associating systems, Biophys. Chem. 159 (2011) 24–32.
[35] M. Sztiller-Sikorska, E. Heyduk, T. Heyduk, Promoter spacer DNA plays an active role in integrating the functional consequences of RNA polymerase contacts with −10 and −35 promoter elements, Biophys. Chem. 159 (2011) 73–81.
[36] Y. Yang, V.J. LiCata, Interactions of replication versus repair DNA substrates with the Pol I DNA polymerases from *Escherichia coli* and *Thermus aquaticus*, Biophys. Chem. 159 (2011) 188–193.
[37] A.G. Kozlov, T.M. Lohman, *E. coli* SSB tetramer binds the first and second molecules of $(dT)_{35}$ with heat capacities of opposite sign, Biophys. Chem. 159 (2011) 48–57.
[38] S. Tungtur, H. Skinner, H. Zhan, L. Swint-Kruse, D. Beckett, *In vivo* tests of thermodynamic models of transcription repressor function, Biophys. Chem. 159 (2011) 142–151.
[39] J. Li, J.C. Lee, Modulation of allosteric behavior through adjustment of the differential stability of the two interacting domains in E. coli cAMP receptor protein, Biophys. Chem. 159 (2011) 210–216.
[40] K.A. Sharp, Allostery in the lac Operon: Population selection or induced dissociation? Biophys. Chem. 159 (2011) 66–72.
[41] S. Khrapunov, M. Brenowitz, Stability, denaturation and refolding of *Mycobacterium tuberculosis* MfpA, a DNA mimicking protein that confers antibiotic resistance, Biophys. Chem. 159 (2011) 33–40.
[42] N. Pozzi, R. Chen, Z. Chen, A. Bah, E. Di Cera, Rigidification of the autolysis loop enhances Na+ binding to thrombin, Biophys. Chem. 159 (2011) 6–13.
[43] M.M. Patel, F. Tzul, G.I. Makhatadze, Equilibrium and kinetic studies of protein cooperativity using urea-induced folding/unfolding of a Ubq–UIM fusion protein, Biophys. Chem. 159 (2011) 58–65.
[44] A. Vitalis, R.V. Pappu, Assessing the contribution of heterogeneous distributions of oligomers to aggregation mechanisms for polyglutamine peptides, Biophys. Chem. 159 (2011) 14–23.
[45] E.J. Danoff, K.G. Fleming, The soluble, periplasmic domain of OmpA folds as an independent unit and displays chaperone activity by reducing the self-association propensity of the unfolded OmpA transmembrane β-barrel, Biophys. Chem. 159 (2011) 194–204.
[46] M.T. Henzl, M.A. Reed, A. Tan, Heightened stability of polcalcin Phl p 7 is correlated with strategic placement of apolar residues, Biophys. Chem. 159 (2011) 110–119.
[47] M. Auton, J. Rösgen, M. Sinev, L.M.F. Holthauzen, D.W. Bolen, Osmolyte effects on protein stability and solubility: A balancing act between backbone and side-chains, Biophys. Chem. 159 (2011) 90–99.
[48] E. Di Cera, Gary K. Ackers (1939–2011), Biophys. Chem. 158 (2011) 90.