14th Annual Gibbs Conference on Biothermodynamics

Touch of Nature Conference Center,
Southern Illinois University
Carbondale, Illinois

Oct. 7th-10th, 2000

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SCIENCE MUSINGS/CHET RAYMO

Painting courtesy/Yale University Archives
Portrait of Josiah Willard Gibbs, eminent scientist.

Meet Mr. Gibbs

A month ago, in a column on the scientific reputation of Benjamin Franklin, I mentioned Willard Gibbs, calling him the greatest scientist America produced until our own century. Several readers asked, "Who's this guy Gibbs you think so much of?" An informal survey confirmed Gibbs' anonymity; no one I questioned could place the man or name his achievements.

Now it turns out we have just celebrated (rather, failed to celebrate) the 150th aniversary of the birth of Josiah Willard Gibbs – on Feb. 11, 1839, in New Haven – so perhaps this is an appropriate time to rescue the great New England scientist from undeserved obscurity.

I am not alone in my estimate of Gibbs' importance. There are those who would say Willard Gibbs is the greatest American scientist of all time. Toward the end of his life, Albert Einstein was asked who he considered the most powerful thinker he had ever met. He answered without hesitation, "Lorentz," referring to Hendrik A. Lorentz, the Dutch mathematical physicist, and then added, "I never met Willard Gibbs; perhaps had I done so, I might have placed him beside Lorentz." High praise indeed from the towering scientific genius of the 20th century.

Years ago, as a graduate student in physics, I kept coming across Gibbs' name – Gibbs' phase rule, Gibbs' paradox, Gibbs free energy, the Gibbs-Helmoltz equation, Gibbs functions, Gibbs ensembles, and so on. The name popped up in texts on chemistry, mathematics, theoretical mechanics, optics and thermodynamics. Sometimes the latter subject seemed entirely a Gibbsian invention.

"He was never in the public eye"

Who was this fellow who was so prolific in shaping so many branches of science? Physicists and chemists acquainted with Gibbs' scientific achievements knew little of the man. Non-scientists did not even recognize the name.

I tracked down Lynde Phelps Wheeler's biography of Gibbs and the first paragraph held the key to his obscurity: "The outward life of Josiah Willard Gibbs was singularly uneventful. He experienced no adventures different from those common to thousands of Americans of his time. He was a participant in no events of historical importance. He took no leading part in any of the movements of the age. He traveled less, and lived at home more, than the great majority of people of similar means. He neither sought nor occupied positions of influence in his own scientific world. He was never in the public eye."

With such a beginning, one may wonder what attracted the biographer to his subject. But the history of civilization is not written only on battlefields and in corridors of power. It is written also in the imagination of men such as Gibbs, who sought and found fundamental principles of physical chemistry and thermodynamics, and who perfected mathematical tools for the exercise of science. Wrote Wheeler: "He explored the far horizons of the hitherto unknown. . .and mapped a major scientific continent."

Gibbs lived in an age of mechanical invention and the raw aggrandizement of power – the age of the transcontinental railroad, the Atlantic cable, the Brooklyn Bridge and the efficient killing technologies of Shiloh and Gettysburg. His own city of New Haven boasted of Charles Goodyear, discoverer of the vulcanization of rubber, Eli Whitney, inventor of the cotton gin and manufacture by interchangeable parts, and Samuel Morse, inventor of the electrical telegraph.

In such a world the abstractions of Willard Gibbs found few admirers. His elegant formulas and equations, couched in mysterious Greek symbols, held little interest for his practical-minded countrymen.

Not that Gibbs' theories were without practical application. Almost every branch of technology ultimately benefited from his work, especially the chemical industry. Alloys, explosives, fuels and medicines were all touched by his genius.

Lived most of life in New Haven

But down-to-earth applications do not seem to have concerned the gentle scholar of New Haven. Except for three years of study in Europe, Gibbs lived all his life in that city, as a bachelor in the home of his sister. He plied his duties as professor at Yale University with quiet dedication, avoiding the spirited debates of university politics. He is remembered at Yale for uncharacteristically standing up at a faculty meeting and saying, to everyone's astonishment in the midst of a curriculum debate, "Mathematics is a language."

As his work became known, universities here and abroad bestowed upon him honorary degrees. He was recipient of the Rumford Medal of the American Academy of Sciences and the Copley Medal of London's Royal Society, the highest honor open to a scientist until the founding of the Nobel Prize. So modestly did Gibbs absorb these accolades that even his friends were unaware of the honors until they read of them in his obituary.

Gibbs' physics was one great cornerstone of 19th century science that survived unscathed the intellectual revolutions of the 20th century. He died in 1903, just two years before Einstein and Max Planck published their epoch-making papers on relativity and quantum physics. These two founders of modern physics were late to discover the work of Gibbs, and consequently, reinvented many of the same results – with *difficulty*. Einstein knew of what he spoke when he placed Gibbs in the highest rank of genius.

Chet Raymo is a professor of physics at Stonehill College and author of several books on science.

14th Annual Gibbs Conference on Biothermodynamics

	Saturday, Oct. 7th
4:00-7:00 pm	Check-in in Indian Room
7:00-10:00 pm	Reception in Indian Room

	Sunday, Oct. 8th
	Keynote
8:30-9:30 am	**Rodney Biltonen** (University of Virginia) *Lateral heterogeneities of membrane lipids, surface distribution of proteins and enzyme function*
9:30-10:00 am	Refreshments
	Session I. Membranes and Membrane Proteins (Moderator: Katherine Tripp)
10:00-10:35 am	**Steve White** (University of California, Irvine) *Folding proteins into membranes: A thermodynamic basis for the prediction of structure from sequence*
10:35-11:10 am	**Cliff Robinson** (3-D Pharmaceuticals) *Molecular biophysics of a G-protein coupled receptor: Determinants of structure, stability and assembly of the β2 Adrenergic receptor.*
11:10-11:30 am	**Xuemei Yang and Allyn Schoeffler** (Louisiana State University) *Ionic effect on lipid binding and stability of adipocyte lipid binding protein*
11:30-12:00 am	**Karen Fleming** (Johns Hopkins University) *Protein-protein interactions in membranes.*
12:00-1:00 pm	Lunch
	Session II Nucleic Acid Structure and Thermodynamics (Moderator: Chin Zou)
3:30-4:10 pm	**Richard Sheardy** (Seton Hall University) *B-Z junctions with mismatched base pairs of T bulges*
4:10-4:30 pm	**Besik Kankia** (Univ. of Nebraska) *Formation of G-quadruplexes with alkaline and alkaline earth metal ions: Folding and hydration*
4:30-5:00 pm	Refreshments
5:00-5:40 pm	**Larry Parkhurst** (University of Nebraska-Lincoln) *Co-solvent and sequence dependent conformational changes when TBP binds to DNA*
5:40-6:00 pm	**Daumantas Matulis** (University of Minnesota) *Thermodynamics of cationic lipid binding to DNA by titration calorimetry*
6:00-7:00 pm	Dinner
8:00-10:00 pm	**Poster Session I**

	Monday, Oct. 9th
	Session III Protein Electrostatics and Dynamics (Moderator: Ana Maria Soto)
8:30-9:10 am	**Don Bashford** (Scripps Research Institute) *Strong electrostatic effects and unusual protonation states in proteins*
9:10-9:50 am	**Bertrand Garcia-Moreno** (Johns Hopkins University) *pKa values of buried groups: Experimental evidence of hydration in the hydrophobic core and implications for pKa calculations with continuum methods*
9:50-10:20 am	Refreshments
10:20-10:40 am	**James Wrabl** (Univ. of Texas Medical Branch) *Determination of thermodynamic propensities of amino acids in protein structures using an ensemble based approach*
10:40-11:20 am	**Andy Robertson** (University of Iowa) *Structural determinants of carboxyl ionization equilibria in proteins*
11:20-12:00 am	**Andrew Lee** (Univ. of Pennsylvania) *Temperature dependence of motional dynamics in a calmodulin-peptide complex*
12:00-1:00 pm	Lunch
	Session IV Nucleic Acid-Protein/Ligand Interactions (Moderator: Luminita Velea)
3:30-4:10 pm	**Gary Stormo** (Washington University) *Pattern recognition methods to infer specificity of DNA binding proteins*
4:10-4:30 pm	**William Peters** (Southern Illinois University) *Intercalation and the energetics of minor groove DNA binding and bending by hyperthermophile protein Sac7d*
4:30-5:00 pm	Refreshments
5:00-5:20 pm	**Gauri Dhaven** (Albert Einstein College of Medicine) *The association kinetics of the integration host factor-DNA complex by time resolved X-ray hydroxyl radical footprinting*
5:20-6:00 pm	**Tomasz Heyduk** (St. Louis University) *Conformation of fork junction DNA in a complex with E. coli RNA polymerase*
6:00-7:00 pm	Dinner
8:00-10:00 pm	**Poster Session II**

	Tuesday, Oct. 10th
	SessionV Protein Folding, Binding and Stability (Moderator: John Satumba)
8:30-9:10 am	**Madeline Shea** (University of Iowa) *Asymmetric Switching of a Symmetric Protein: Exploring the Allosteric Mechanism of Calmodulin*
9:10-9:30 am	**Alexandra Klinger** (Washington University) *Non-cooperative O_2 binding to the α–α and β–β subunit pairs within the human hemoglobin tetramer supports the symmetry rule mechanism*
9:30-10:00 am	Refreshments
10:00-10:40 am	**Michael Fried** (Penn State Coll. of Medicine) *In vitro interaction of the E. coli cyclic AMP receptor protein with the lactose repressor.*
10:40-11:20 am	**Walter Englander** (Univ. of Pennsylvania) *Two-state vs. multistate protein unfolding studied by classical melting analysis and hydrogen exchange*
11:30-12:30 pm	Lunch
12:30 pm	**Check-out and Departure**

Poster Information

Posters will be presented in one of two sessions, I and II, to be held Sunday and Monday evenings, respectively, in Sledgefoot Hall (Next to Freeberg, the dining hall).

Session I: First Authors **A** through **M**. Posters may be mounted starting on Sunday morning.

Session II: First Authors **N** through **Z**. Posters may be mounted starting on Monday morning.

Posters I, alphabetical by first Author

Sunday 8-10pm, Sledgefoot Hall

The Dominant Pathway in the Hemoglobin O_2 Binding Cascade Passes Through the $\alpha^1\beta^1$ Half-Oxygenated Intermediate

Gary K. Ackers*, Jo M. Holt & Alexandra L. Klinger

The SlyD peptidyl-prolyl isomerase from E. coli accelerates folding and assembly of lambda Cro dimers

Ibrahim Al-Duraibi,* Melva James, and Michael C. Mossing.

Continuum and atomistic treatment of ion solvation in synthetic ion channels

D. Asthagiri* and D. Bashford

Differential Thermodynamic Focusing in a TCR/peptide/MHC Interface: a Geometrical Requirement for TCR Signaling?

Brian M. Baker[1*], William E. Biddison[2], & Don C. Wiley[1]

Equilibrium Unfolding Studies of the *E. coli* periplasmic chaperone PapD

James G. Bann[*1], Jerome Pinkner[2], Scott J. Hultgren[2], and Carl Frieden[1]

The Role of Protein Partners in Modulating Ultrabithorax Function

Sarah E. Bondos*, Xin-Xing Tan, Kathleen S. Matthews

Limited Proteolysis and MALDI-TOF Mass Spectrometric Analysis of Procaspase-3

Kakoli Bose and A. Clay Clark*

Hinge Helix Folding and the Allosteric Transition of the Lactose Repressor

Michelle Calabretta* and Kathleen Shive Matthews

Folding and Assembly of the Caspase-3 Subunits

*Yun-Ru Chen** & *A. Clay Clark*, Department of Biochemistry,

Equilibrium Folding of Procaspase-3

*A. Clay Clark** & *Randy Durren*, Department of Biochemistry,

Linkage of Protonation of Specific Sites to the Folding of the Hyperthermophile Protein Sac7d

Andrew Clark*, Nicholas Szary, Gabe Shaughnessy, Stephen Edmondson, John Shriver

Synthesis and Initial Characterization of Potential Telomerase Inhibitors

Nancy Coffman*, Scott Petrich* and Susan Pedigo[+]

Sedimentation Studies Reveal a Direct Role of Phosphorylation in Smad3:Smad4 Homo- and Hetero-Trimerization. **John J. Correia[*]**, Benoy M. Chacko[+], Suvana S. Lam[+], and Kai Lin[+]. [*]Department of Biochemistry, University of

The effect of GroES and nucleotides on GroEL mediated refolding of *E. coli* DHFR

TU ANH T. DANG* and CARL FRIEDEN

Investigation into the Effects of Multi-Site Proton Linkage on Isothermal Titration Calorimetry Data

Stephen P. Edgcomb* & Kenneth P. Murphy

"Trypsin's and Subtilisin's Similar Binding Sites Explained with Extensive Orbital Steering." *Y.-H. Fan and J. Haseltine*, Département de chimie, Université de*

Solution Structure and the Ligand Binding Site of the Sem-5 SH3 domain

Josephine C. Ferreon*, David E. Volk, Bruce A. Luxon, David G. Gorenstein and Vincent J. Hilser

Dimerization and subunit exchange of lambda Cro by fluorescence resonance energy transfer

Garrick L. Florence*, Alexander E. Fong and Michael C. Mossing.

Target Recognition by Human S100P: Ca^{2+} and Mg^{2+}-Dependent Interactions with Amphipathic Peptide Melittin†

Alexey V. Gribenko and George I. Makhatadze*

Transcriptional Control of the *gcvTHP* Operon, Encoding the Glycine Cleavage Enzyme System in *Escherichia coli*: Evidence for Linked Equilibria Among Several Regulatory Components

Gary Heil* (gary-heil@uiowa.edu), Andrew Robertson‡ and George V. Stauffer

ISOFORM-DEPENDENT IMPACT OF MONOVALENT CATIONS ON PARVALBUMIN DIVALENT ION AFFINITY

Michael T. Henzl*, John D. Larson, and Sayeh Agah

COMPARISONS BETWEEN VAN'T HOFF AND CALORIMETRIC ENTHALPIES USING ISOTHERMAL TITRATION CALORIMETRY

James R. Horn[1,*], Donald L. Russell[2], Edwin A. Lewis[2], John F. Brandts[3], and Kenneth P. Murphy[1]

ROLE OF ELECTROSTATIC INTERACTIONS IN THE STABILITY AND FOLDING/UNFOLDING REACTIONS OF THE COILED-COIL PEPTIDE GCN4-p1

Beatriz Ibarra-Molero* and C. Robert Matthews

Do ΔC_p and m values relate to the same change in solvent accessible surface area upon unfolding?

Sandhya Jain[1*], Kevin L.Shaw[2], C.Nick Pace[2] and Kenneth Murphy[1]

Calcium-Induced Conformational Switching in *Paramecium* Calmodulin Varies With Location in the Structure and is Altered by Mutations

Olav R. Jaren[1]*, James K. Kranz[2], Brenda R. Sorensen[1], A. Joshua Wand[2], and Madeline A. Shea[1]

Protein Stability Surface for Sac7d by Hydrogen Exchange

Mebrahtu Kahsai, Stephen P. Edmondson, John W. Shriver

Proline-Rich Regions of Sequence: The Polyproline II Helix

Melissa Kelly and Trevor P. Creamer*

Hydrostatic Pressure Used as a Probe of Molecular Recognition in the Calmodulin:smMLCK Complex

*James K. Kranz & A. Joshua Wand

NMR and computational study of the effects of salt on pK_a values: long-range electrostatic interactions in staphylococcal nuclease are substantial

Kelly K. Lee, Carolyn A. Fitch, and Bertrand García-Moreno E.

Domain Stability and DNA Recognition in *E.coli* CRP

Jianquan Li*, Shwu-Hwa Lin and J. Ching Lee, Department of Human Biological

Engineering A Thermostable Protein via Optimization of Charge-Charge Interactions on the Protein Surface

Vakhtang V. Loladze[‡], Beatriz Ibarra-Molero[§], Jose M. Sanchez-Ruiz[§], George I. Makhatadze*[‡]*

THERMODYNAMICS OF AN INTRAMOLECULAR DNA TRIPLE HELIX WITH SEQUENCE: d(AGAGAC_5TCTCTC_5TCTCT)

Jacqueline Loo, Ana Maria Soto and Luis A. Marky*

INTERACTION OF DISTAMYCIN WITH DNA OLIGOMERS CONTAINING ONE A_3T_2 BINDING SITE: CONTRIBUTION OF SECONDARY STRUCTURE.

Souvik Maiti*, Besik I. Kankia and Luis A. Marky

Comparison of Sodium Perchlorate, Guanidine-Hydrochloride and Urea Induced Unfolding of *Staphylococcal* Nuclease, Its V66W Mutant and V66W' Fragment: Evidence for Multiple Equilibrium Intermediates

Haripada Maity, Numukunda Darboe and Maurice R. Eftink

Conformational Changes of the Seven-Transmembrane Protein, Bacteriorhodopsin

Martinez, LC and Turner, GJ. University of Miami School of Medicine, Miami, FL

Posters II, alphabetical by first Author

Monday 8-10pm, Sledgefoot Hall

Simulation of NMR Order Parameters in a Calmodulin-Peptide Complex

*Hongkang Mei, Kim Sharp**

Staphylococcal Nuclease Mutants I92E and I92K Contain Deeply Buried Ionizable Side Chains that Sense Effective Dielectric Constants of 10 to 15

Duc Nguyen, Eaton Lattman, and Apostolos Gittis

Role of promoter elements for specific binding of sigma ^{70} containing RNA polymerase holoenzyme

Anita Niedziela-Majka* and Tomasz Heyduk

A single residue participating in a non-native interaction is responsible for superprotection in *E. coli* HPr

Ronald W. Peterson* and J. Martin Scholtz

Attenuation of GCSF Aggregation by Naturally Occurring Osmolytes

*Youxing Qu * and Wayne Bolen*

Coupled Plasmon Waveguide Resonance Spectroscopy
Glen Ramsay

Mechanistic Studies of Inhibition of RSV Fusion in the Presence of WAY-154641

Vladimir Razinkov*, Anna Gazumyan, George Ellestad and Girija Krishnamurthy

Thermodynamics of Helix Unfolding

John M. Richardson and George I. Makhatadze

How is the ability of an osmolyte to protect proteins from different denaturing stresses related to its evolutionary origins?

Andrew T. Russo, Ilia V. Baskakov, and Wayne Bolen

Proline isomerization limits folding and assembly kinetics of lambda Cro dimers

John W. Satumba* and Michael C. Mossing.

Increasing the conformational stability of globular proteins

David Schell, Stephanie B. Newsom, Saul Trevino & C. Nick Pace

THERMODYNAMICS OF DNA HAIRPIN LOOPS: LOOP-STEM STACKING CONTRIBUTIONS

Ronald A. Shikiya* and Luis A. Marky

Investigation of a Hydrogen Bond Network

*Jason P. Schmittschmitt * & Martin J. Scholtz*

EX1 Hydrogen Exchange in Ubiquitin

T. Sivaraman*, Cammon B. Arrington & Andrew D. Robertson

Calcium-dependence of Melittin Binding to *Paramecium* Calmodulin is Domain Specific and Altered by Mutations

Brenda Sorensen*, Wendy VanScyoc, Jason-Thomas Eppel, and Madeline A. Shea

THERMODYNAMIC EFFECTS RESULTING FROM THE INCORPORATION OF MODIFIED URIDINES IN DNA OLIGOMER DUPLEXES

Ana Maria Soto*, Prasad Dande, Barry Gold and Luis A. Marky

Global Non-Linear Curve Fitting to Time Difference Sedimentation Velocity data: Determination of Equilibrium Constants of Heterologous Interacting Systems with Accompanying Self-association.

Walter F. Stafford

Bacteriorhodospin stretched to the limit: An AFM analysis of BR conformers

Studer, S, Benitez, I, Moy, V, Levay, A, Wojcikiewicz, E, and Turner, GJ. University of Miami School of Medicine, Miami, FL

Plasticity of Quaternary Structure: Twenty-two Ways to Form a LacI Dimer.

Liskin Swint-Kruse[1,2], Corey Rayne Elam[2], Jennifer W. Lin[2], Diane R. Wycuff[2,3], and Kathleen Shive Matthews[1,2]

1[illegible]

Multiple Facets of Ultrabithorax: A Protein Linkage Map

Xin-Xing Tan*, Sarah E. Bondos, and Kathleen S. Matthews

pKa Determinations of Histidine Variants of Ribonuclease Sa

Richard L. Thurlkill*, Beatrice M.P. Huyghues-Despointes, J. Martin Scholtz, C. Nick Pace

A New Linear Ising Model of Cooperative Myosin-Thin Filament Binding. Analysis of the Thin Filament as a Large Allosteric System

Larry Tobacman*, Carol Butters, Earl Homsher, Roger Craig, and William Lehman

Structure, Stability, and Calcium Binding Properties of N-domain Mutants of *Paramecium* Calmodulin

Wendy Van Scyoc*, Laurel Coffeen, and Madeline A. Shea

ABSTRACT

INTERACTIONS OF ACRIDINE-BASED ANTICANCER AGENTS WITH DNA: CONSIDERATION OF LIGAND DESIGN IN DIRECTING DNA BINDING ENERGETICS

Luminita M. Velea, Murrell Godfrey, Steven Stricker, Rachel Hutchins and David Graves

Unstructured Regions Contribute to Stability and Kinetics of Protein Unfolding

Travis T. Waldron*, Stephen P. Edgecomb, Sandhya Jain, Kenneth P. Murphy

Corepressor-induced Assembly of a Dimerization Interface in the Biotin Repressor
L.H. Weaver[2], K.H. Kwon[1], D. Beckett[1], B. Matthews[1], [1]Department of Chemistry and

The origin of pH-dependent changes in *m*-values for the denaturant-induced unfolding of proteins.

Steven T. Whitten*[¶], John, O. Wooll[¶], Reza Razeghifard[¶], Bertrand Garcia-Moreno E[†]. and Vincent J. Hilser[¶]

Ensemble Modulation as an Origin of Denaturant-Independent Hydrogen Exchange in Proteins

John O. Wooll* James O. Wrabl, and Vincent J. Hilser

Protein Fold Recognition Using Ensemble-Based Structural Thermodynamics

James O. Wrabl, Scott A. Larson*, and Vincent J. Hilser

Predicting Free Energy Landscapes of Complexes of Double-Stranded Chain Molecules Wenbing Zhang[1] and Shi-Jie Chen[1,2], Department of Physics[1] and De-

Thermodynamics of the Interactions between TFE and Protein Functional Groups
Qin Zou* and Kenneth P. Murphy

A novel energy function for ligand-protein interactions with applications to interactions of potassium channels with their known extracellular-entryway blockers. Xiaoqin Zou, Dalton Cardiovascular Research Center and Department of Biochemistry,

STABILITY AND INTERACTIONS OF THE ANKYRIN REPEATS OF THE NOTCH RECEPTOR

Mark Zweifel* and Doug Barrick