The Gary K. Ackers Lecture in Biothermodynamics

Inaugural Lecturer (2009): Michael D. Brenowitz, Albert Einstein College of Medicine

This lecture honors the scientific contributions of Gary K. Ackers to the field of Biological Thermodynamics. Gary is a Professor Emeritus of the Washington University School of Medicine, and Fellow of the Biophysical Society.

Gary has demonstrated a lifelong commitment to the growth and development of an intellectual community of scholars devoted to furthering the field of biothermodynamics. Gary has been an active member of the Biophysical Society throughout his career and has served as President of the Society, as well as Organizer of the annual meeting. While on the faculty of the University of Virginia, he was a leader in the graduate biophysics training program. When on the faculty in the Department of Biology at the Johns Hopkins University, he conceived and organized the Institute for Biophysical Studies of Macromolecular Assemblies, a university-wide training program in molecular biophysics that has continued for decades. While at Johns Hopkins, he also played a leading role in the establishment of the Gibbs Conference on Biothermodynamics, an annual meeting organized to promote innovative development of biophysical principles applied to current problems in biology and to train the next generation of molecular biophysicists to tackle hard problems rigorously. After moving to St. Louis to chair the Department of Biochemistry and Molecular Biophysics at Washington University, he spearheaded a new graduate program in biophysics and hired many faculty who have joined the community of regular contributors to the Gibbs Conference.

Gary was a pioneer in the development of methods and application of principles of equilibrium thermodynamics to the study of linkage in complex macromolecular assemblies. Studies from his laboratory on the energetics of self-association and ligand binding in human hemoglobin proved unequivocally that the classic and elegant MWC model of intersubunit allostery was insufficient to explain cooperative oxygen binding: the position, as well as the number, of ligands matters. His contributions in this area greatly enhanced our understanding of the relationship between structure, energy and function in hemoglobin, and in multimeric allosteric systems in general. By probing ever more deeply into the molecular mechanism of cooperativity, he demonstrated a beautiful, useful, and general strategy for dissecting functional energetics in macromolecular assemblies.

His quantitative study of the interactions between proteins and nucleic acids in the bacteriophage lambda system included the development of quantitative DNase footprinting methods for measuring free energies of repressor-operator interactions. The footprinting assay remains an effective tool for measuring the extremely tight binding constants that are often encountered in site-specific interactions between proteins and nucleic acids. Those studies paved the way for similar methods to study protein-nucleic acid interactions in more complex systems, including time-resolved studies of the kinetics of RNA folding. Based on his experimental studies of phage lambda, his group developed statistical thermodynamic models to simulate the lysogenic-to-lytic growth switch: the series of macromolecular events that determine the fate of bacteriophage lambda during infection of E. Coli. This work demonstrated how a complex biological function could be predicted quantitatively, strictly from the kinetics of transcription and translation, and the Gibbs free energy of interactions between the key macromolecular components in the genetic switch.

During Gary's early career, he developed methods to measure association constants in self-associating systems based on analytical gel permeation chromatography. Those methods have since become standard tools in the field. His group was also responsible for modifications of the cryo-gel electrophoresis methods, moving from applying them to hemoglobin to protein- DNA interactions. These contributions focused on developing the capacity to quantify intermediate states that are only transiently populated during the course of a biochemical process. His more than 200 articles and chapters changed our view of the molecular mechanisms that govern complex biochemical reactions.

Meeting schedule

Saturday, October 3

4:00-7:00 pm Check-in at Little Grassy Lodge
7:00-10:00 pm Reception in Indian Room. Light refreshments/drinks.

Sunday, October 4

8:45-8:50 am Welcome: Luis Marky, Gibbs Society President
8:50-8:55 am Administrivia: Liskin Swint-Kruse and Nathan Baker

Macromolecular assemblies and interactions

Moderator: Phillip K. Veronese, Lucius Lab, University of Alabama at Birmingham
8:55 am Keynote introduction: Tim Lohman, Washington University in St. Louis
8:55-9:55 am Keynote: "Molecular interpretations of heat capacity change in macromolecular interactions", Linda Jen-Jacobson, Univ. of Pittsburgh
9:55-10:15 am "Correlating thermodynamics of DNA binding with functional behavior of DNA polymerases", Hiromi Brown, LiCata lab, Louisiana State University

10:15-10:45 am *Refreshment break*

10:45-11:05 am "Structure, function and dynamics of the Pitx2 homeodomain", Thomas Doerdelman, Rance lab, University of Cincinnati
11:05-11:40 am "TBA", Wlodek Bujalowski, University of Texas Medical Branch at Galveston
11:40-12:00 pm "Dynamic imaging of restriction enzyme interactions with DNA using high speed atomic force microscopy", Jamie Gilmore, Lyubchenko lab, University of Nebraska Medical Center

12:10 pm *Group photo and lunch*

Protein structure and function I

Moderator: Aaron C. Robinson, Garcia-Moreno lab, Johns Hopkins University
3:00-3:35 pm "Universal convergence of the specific volume changes of globular proteins upon unfolding", George Makhatadze, Rensselaer Polytechnic Institute
3:35-3:55 pm "Allosteric mechanism of hexameric arginine repressor", Rebecca Strawn, Carey lab, Princeton University

3:55-4:25 pm *Refreshment break*

4:25-5:00 pm "Folding histones: dimers in action", Lisa Gloss, Washington State University
5:00-5:20 pm "Rapid biophysical characterization of nanogram quantities of protein", Daniel Isom, Hellinga lab, Duke University
5:20-5:55 pm "Conformational equilibria of intrinsically disordered polypeptides", Rohit Pappu, Washington University in St. Louis

6:00 pm *Dinner*

Data fitting workshop

7:15-8:00 pm "Fitting equations to experimental data", Michael Johnson, Univ. of Virginia

Poster session I

8:00 pm First authors with last names starting with M-Z

Monday, October 5

8:40-8:45 am Administrivia: Liskin Swint-Kruse and Nathan Baker

Nucleic acid structure and function

Moderator: Colin G. Wu, Lohman lab, Washington University in St. Louis

8:45 am The Gary K. Ackers Lecture in Biothermodynamics introduction: James C. Lee, University of Texas Medical Branch at Galveston

8:45-9:45 am The Gary K. Ackers Lecture in Biothermodynamics: "Finding the roads most traveled during RNA folding", Michael Brenowitz, Albert Einstein College of Medicine

9:45-10:05 am "Tertiary contacts modulate the energy landscape of a bacterial group I ribozyme", Reza Behrouzi, Woodson lab, Johns Hopkins University

10:05-10:25 am "Enhancement of fluorescence from nucleoside analog 6MI through specific DNA pentamer Sequence ATFAA", Andrew Moreno, Mukerji lab, Wesleyan University

10:25-10:55 am *Refreshment break*

10:55-11:30 am "Ion-nucleic acid interactions and RNA folding", Lois Pollack, Cornell University

11:30-11:50 am "Prediction of Hofmeister ion effects on biopolymer processes", Laurel Pegram, Record lab, University of Wisconsin Madison

11:50-12:25 pm "What makes DNA stiff and what do cells do about it?", Jim Maher, Mayo Clinic

12:30 pm *Lunch and business meeting*

Membrane assemblies and proteins

Moderator: Yogini Bhavsar, Pedigo Lab, University of Mississippi

3:00-3:20 pm "Arginine insertion into phospholipid membranes: effects on the folding and functioning of a membrane protein", Preston Moon, Fleming lab, Johns Hopkins University

3:20-3:55 pm "Weak interactions at the membrane are advantageous for a discriminating response in signaling", Anne Hinderliter, University of Minnesota Duluth

3:55-4:15 pm "Monitoring membrane protein unfolding by pulse proteolysis", Jonathan Schlebach, Park lab, Purdue University

4:15-4:45 pm *Refreshment break*

4:45-5:20 pm "Is it possible to measure thermodynamic stability of membrane proteins in a lipid bilayer environment?", Alex Ladokhin, Kansas Univ. Medical Center

5:20-5:40 pm "Modeling a contact-facilitated delivery mechanism of PFOB-based nanoemulsions by molecular dynamics simulations", Sunjoo Lee, N. Baker lab, Washington University in St. Louis

5:40-6:15 pm "Toward design rules for antimicrobials, cell penetrating peptides, and pore forming proteins", Gerard Wong, University of Illinois Urbana-Champaign

6:20 pm *Dinner*

Fluorescence workshop

7:20-7:40 pm "Time-Resolved Stopped-Flow Fluorescence". Jim Mattheis, HORIBA Scientific

7:40-8:00 pm "AUC fluorescence detection system progress", Glen Ramsay, Aviv Biomedical, Inc.

Poster session II

8:00 pm First authors with last names starting with A-L

Tuesday, October 6

8:40-8:45 am Administrivia: Liskin Swint-Kruse and Nathan Baker

Protein structure and function II

Moderator: Matthew Preimesberger, Lecomte lab, Johns Hopkins University

8:45-9:20 am "Folding and assembly of procaspase-3: the role of the dimer interface in active site formation", Clay Clark, North Carolina State University

9:20-9:55 am "Poly-bivalency in the assembly of intrinsically disordered proteins", Elisar Barbar, Oregon State University

9:55-10:15 am "Determinants of intrinsic and interfacial effects in repeat protein folding", Tural Aksel, Barrick lab, Johns Hopkins University

10:15-10:35 am *Refreshment break*

10:35-10:55 am "Thermodynamic mechanism of the ionic strength-induced cooperativity changes in the cyclic AMP receptor protein", Alexey Gribenko, J. Lee lab, University of Texas Medical Branch

10:55-11:30 am "Uncovering specific electrostatic interactions in the denatured state of proteins", Jana K. Shen, University of Oklahoma

11:30-12:05 pm "Protein folding kinetics versus thermodynamics: a play in two acts", Patricia Clark, University of Notre Dame

12:10 pm *Box lunch and departure*