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INTRODUCTION

Foreword to the biophysics of protein-protein and protein-ligand interactions in dilute and crowded media—a special issue in honor of Allen Minton's 70th birthday

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Allen Minton of the National Institutes of Health, has arguably been one of the most innovative biophysical scientists of the last 50 years. Conducting his research career over a diverse range of topics, Allen's contributions have oftentimes come to define the areas in which he has worked. A good example of this point is provided by Allen's studies of the behavior of biomolecules in extremely concentrated biological solution environments, such as those existing within the cell—an area that has come to be known as macromolecular crowding. This year Allen Minton turns 70 years old. To mark the occasion we suggested to him that a special issue in Biophysical Reviews, the official IUPAB (International Union of Pure and Applied Biophysics) review journal might be a suitable way of recognizing the event. Initially he rejected the idea as representing an unnecessary fuss. However with a little persistence we eventually received from him a list of names of people he might like to contribute—together their work constitutes the basis of this edition of the Biophysical Reviews journal. Our apologies to those not appearing in this special issue due to either space or time limitations.

Special Issue: Protein-Protein and Protein-Ligand Interactions in Dilute and Crowded Solution Conditions. In Honor of Allen Minton's 70th Birthday

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In this foreword we would like to say a few words about Allen, giving a short review of his life in and out of science. We will then provide a description of the theme of this special issue and the individual articles contained within it. The prefatory material will conclude with a short piece by Allen, expressing his thanks to colleagues and contributors, as well as offering a few thoughts on science and life.

Early Life and University[1]: Allen was born on July 5th, 1943 to a middle class family in Washington, D.C. His father was a lawyer, his mother a home maker and part-time music teacher. Allen had two younger brothers, Jules, who became a writer for television and motion pictures, and Kenneth, who became a renowned expert on the molecular mechanism of DNA repair. When he was an infant, his family moved to the west coast to chase a business opportunity and as a result Allen grew up in Los Angeles. As a child of the Sputnik era he was fascinated by science and developed a keen interest in electronics and physics. Indeed the introductory chapter from Richard Feynman's biography (Feynman and Leighton 1985) 'He fixes radios by thinking' seems to be equally applicable to Allen's childhood endeavors. A top student at school Allen was accepted into the University of California, Los Angeles, where he studied a broad based degree in the physical sciences, graduating with very highest honors in chemistry in 1964. Indeed Allen was such a good student that upon graduating he was pursued by the Nobel Prize winning chemist Willard Libby to join his laboratory. To quote Allen,

> As a young scientist there is nothing that can raise your spirits more than having a Nobel prize winner explain to you why you should come to his laboratory and not go to that of another Professor.

[1] The basis for this section comes from many conversations with A.P.M. and from a special interview conducted during 2012 (quite appropriately standing next to an analytical ultracentrifuge).

Allen conducted his Ph.D. with Libby studying the microwave spectrum of hemes in hemoglobin theoretically and experimentally. True to form Allen performed theoretical calculations and built much of the equipment used to perform his experiments. This practical side of Allen, as someone willing to tackle both theory and experiment (and someone who was highly capable in both areas) would be an ongoing theme of Allen's work throughout his research career.

Time at the Weizmann: Soon after the award of his Ph.D. Allen started his first postdoctoral fellowship with Prof. Henryk Eisenberg at the Weizmann Institute in Rehovoth Israel. During this time he concentrated his research studies on quantum calculations of condensed water phases and was one of the first chemists to question the veracity (Minton 1970) of the quantum basis of the polywater phenomenon originally advanced by Deryagin et al. (1965). Outside of the laboratory Allen met and fell in love with, 'a very beautiful young lady', Sima, whom he subsequently asked, and received, permission to marry. During his time at the Weizmann Institute Allen was exposed to a lot of the biophysical theory and measurement techniques he would later go on to make major advances in—such as chromatography (Minton 1980), viscosity (Ross and Minton 1977a), analytical ultracentrifugation (Minton 1992a) and light scattering (Attri and Minton 2005).

Harry Saroff and the NIH: Returning to the USA with his new bride in tow Allen started work at the National Institutes of Health in Bethesda Maryland, working as a Staff Fellow in what was then known as the National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases (NIADDKD)[2] within the laboratory of Dr. Harry Saroff[3]. As one of the original fellows in the laboratory of Edwin Cohn at Harvard, Harry Saroff could trace his scientific origins back to the beginnings of protein biophysical chemistry in America. Harry's mentorship, along with that provided by the many other great scientists working at the NIH, provided a research environment with a strong sense of historical perspective and commitment to scholarship—features that are synonymous with Allen's character and work. In Harry's lab Allen began to seriously explore the topic of Hemoglobin allostery (Saroff and Minton 1972; Minton and Saroff 1974).

Independent Section Chief: After 4 years in Harry Saroff's lab Allen was promoted to Senior Investigator and then to Chief of the Section on Physical Biochemistry, the position he still holds to this day. During this time Allen made a number of groundbreaking discoveries in the areas represented in this special issue.

Macromolecular crowding: Continuing on with his hemoglobin studies Allen investigated the effects of highly concentrated protein solutions, such as might be found in the red blood cell, on hemoglobin structure and function. Approaching the topic obliquely, Allen applied hard particle equation of state theories to quantitatively interpret his experimental measurements of Hemoglobin behavior at concentrations of ~400 mg/ml and ~30–40 % volume occupation (Minton 1977; Ross and Minton 1977b). This approach literally revolutionized a field that had previously been limited to simple treatments of non-ideality described in terms of the second-virial coefficient. Allen extended this basic approach to provide insight into areas as diverse as macromolecular diffusion (Muramatsu and Minton 1988), enzyme kinetics (Minton and Wilf 1981), protein adsorption (Chatelier and Minton 1996) and nanotechnology (Minton 1992b). These pioneering theoretical and experimental approaches (along with the terminology of 'macromolecular crowding' that Allen coined) were adopted as the new paradigm for interpretation and testing of biochemical behavior in concentrated solutions of proteins and sugars (Zimmerman and Minton 1993).

Analytical ultracentrifugation: In the modern era of analytical ultracentrifugation, which began with the release of the XL-A by Spinco/Beckman in the latter part of the 1980's., Allen was an early developer of both hardware and software. He constructed the first fully automated data capture and analysis system for the older Model E centrifuge in the early 1970s, and subsequently wrote the initial data analysis software for the XL-A. Together with a number of collaborators, Allen pioneered the use of preparative ultracentrifuges for analytical studies of tracer sedimentation equilibrium (Rivas et al. 1999), inventing and patenting the automated fraction collector along the way (Attri and Minton 1984).

Light Scattering: Over the last ten years Allen has helped to develop theory, instruments and techniques for the rapid determination of macromolecular association stoichiometries and equilibrium constants using both multi-angle laser light scattering and dynamic light scattering devices (Attri and Minton 2005). A feature of this methodology has been the extremely rapid and robust characterization of reversible macromolecular interactions using composite gradient approaches (Attri et al. 2010, Martos et al. 2010). Working in close collaboration with the Wyatt Technology Corporation, Allen's methodology has been commercialized under the commercial name of Calypso™.

[2] The NIADDKD has since become the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK).

[3] We can imagine what an exciting time this must have been for Allen as Harry was truly not only a great scientist, gifted in mathematics, physics, chemistry and biochemistry, but also an exemplar role model in how to live an honorable life whilst attempting to extract the maximum amount of fun.

Biophysical Modeling: Allen has been active in helping colleagues in their attempts to simplify complex data via the application of physical modeling approaches. With regard to these endeavors he has helped to make considerable breakthroughs in the fields of cell volume regulation (Minton et al. 1992), cytoskeletal biology (Hall and Minton 2005), protein chaperone action (Hayer-Hartl and Minton 2006) and amyloid formation (Ross et al. 2005). An early pioneer of the application of physical methods for data reduction and analysis to biochemical data and via his teaching duties at the NIH he trained many of the scientists who later became prominent in the field of quantitative biology.

Other qualities: Allen has been a much treasured colleague within the NIH community and amongst biophysical chemists worldwide conducting research in related research areas. Part of the reason why he has been admired by many has been the highly ethical approach in which he has carried out his science. His generosity with junior colleagues is famous, encouraging many of the people who have worked in his laboratory to publish independently if he deemed his contribution to be limited to guidance and encouragement (which it almost never was). Allen's dislike of appending his name to articles in which he was not an active participant has kept his total paper count modest by today's standards yet it has also meant that each article in Allen's authorship list carries the imprint of his thinking and evidence of his toil. His scientific integrity also extended to practicing concepts associated with scientific sustainability (Minton 1996). Taking and training only a few postdoctoral fellows at a time, Allen's lab has never extended much beyond a group of five, oftentimes being much smaller than this. His collegial nature has been demonstrated by a lifetime of involvement with local and international scientific bodies. These efforts, along with his maintenance of several long term collaborations, have made Allen a friend to many in the scientific community. However the principal reason for the scientific longevity of Dr. A.P. Minton has been the consistently high quality substantive science, frequently as the sole researcher/author, that he has published each year, over the last 50 years. Such a lifetime of concentrated effort has demonstrated that he is a scientist of remarkable intellect and imagination. Perhaps we can offer no greater complement than saying that we, like many others, have enjoyed reading his papers for these reasons.

Summary: This year, 2013, marks the 70th birthday of Allen Minton. To mark the year of his birthday, this special edition festschrift of Biophysical Reviews has been assembled by colleagues and peers working in some of the areas Allen has contributed to over his long career. Due to the breadth of his research over the last 50 years this special issue has, of necessity, included a diverse range of research topics related to biophysical methodology and biophysical theory. We finally settled on the thematic issue title of 'Biophysics of protein-protein and protein-ligand interactions in dilute and crowded media: A special Issue in honor of Allen Minton's 70th birthday'. On behalf of all of the contributors we sincerely wish you a happy 70th birthday.

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