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Walter Kauzmann's contributions to the future of science: a personal recollection

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'When not challenged by the need to understand seemingly incompatible observations, my mind goes easy on itself. A very strong incentive for coming to grips with intellectual puzzles is the need to lecture about them.' James D. Watson, 2002

Walter Kauzmann was already a senior distinguished professor in Princeton University's Department of Chemistry when I arrived as a 28-year-old Assistant Professor of Chemistry in the fall of 1966. As my first teaching assignment, the next year I was to take full responsibility for one of the three core courses for graduate students interested in biochemistry: Chemistry 542, Macromolecular Chemistry. Like the other two core courses, my course was to be taught 5 days a week for 8 weeks. The official textbook was Charles Tanford's *The Physical Chemistry of Macromolecules* [6], but only a fraction of the course material was covered by this text.

The class that I taught was taken for credit by a mixture of first-year graduate students and advanced undergraduates. Many were outstanding young people who have gone on to become leaders in chemistry, biochemistry or cell biology. I quickly discovered how difficult it would be to prepare 40 lectures, plus problem sets and exams, for a course that I had never taught previously. Much of the course—after my carefully prepared initial lectures—would end up being made up on the fly. Because of the 5 day a week schedule, I found that I could usually prepare only Monday and Tuesday's lectures on the preceding weekend. And, even though I did nothing else for 8 weeks, I almost always had to stay up all Thursday night to prepare Friday morning's lecture. I discovered coffee, and it was the strain of teaching this course that initiated my 35-year history of caffeine addiction.

Although I had taken several advanced physical chemistry courses, and Harvard's Chemistry 60 had been my favorite course as an undergraduate, I found that I was learning much of the material that I was teaching for the first time. Two important sources for me were Walter's beautiful 300-page book called *Thermodynamics and Statistics* [5] and his famous review of hydrophobic forces in *Advances in Protein Chemistry* [3]. But I often ran out of time to fix whatever confusion was left from my readings. Then Walter could be relied on to set me straight, invariably being willing to take time off from whatever he was doing to help me out.

Amazingly, Walter never felt that he was too busy for these tasks; in fact, he even seemed to enjoy them. I especially remember one very long session, that followed a knock on his office door to ask for help in calculating the effect of varying the length of an invisible string of zero mass—one that connects two identical spheres—on the sedimentation rate of the joined pair of spheres in an ultracentrifuge. The calculation had stymied me,

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but I felt that understanding it could clarify the whole subject of frictional coefficients for the students. Walter seemed amused, and without ever looking at any of the hundreds of books in his office, he proceeded to work out the answer on the blackboard starting from a few basic principles of physics. Two hours later I emerged from his office exhilarated, with a new appreciation for the role of physics for my own field of molecular biology.

I am sure that I learned more from teaching that physical chemistry course—much either from Walter himself or from his writings—than any of the students who took it. Thus, for example, a fundamental relationship in physics and chemistry is expressed through the Boltzmann distribution; this directly connects the relative probability of two states to the energy difference between them, as a function of the absolute temperature. The almost magical connection between probabilities, energy, and temperature had been simply presented as a fact during my own studies. But in Walter's book it was carefully derived and explained in a 76-page chapter on 'The Molecular Interpretation of Entropy'. Naturally, I could not resist passing this exciting personal discovery on to my students.

Every year I found that the students in the course, who had excelled in their studies, had previously 'mastered' the concept of Gibbs free energy without really understanding it. Again, Walter's little book came to the rescue, allowing me to show how the change in this free energy provides a clever accounting device—one that directly represents the entropy change of the universe for a reaction in an enclosed system at constant temperature and pressure. The importance of students grasping this fact, and its centrality for any understanding of living systems, explains the inclusion of a dense two-page panel on 'Free Energy and Biological Reactions' in our own textbook, the *Molecular Biology of the Cell*, now in its 4th edition [1].

In his introduction to *Thermodynamics and Statistics*, Walter writes: 'The principles that form the basis of thermodynamics and statistical mechanics are beautifully simple, and the mathematical consequence of these basic principles are powerful, extensive and elegant.' It is a pity that, in their probing of details at the frontiers of knowledge, scientists so often lose track of the beauty. What our predecessors have accomplished in creating a profound understanding of the natural world is truly amazing. If I try hard, I can vaguely remember the thrill, 44 years ago, of suddenly realizing that we humans had been able to decipher the details of molecular interactions we could not see directly—simply by analyzing a set of physical chemical measurements of observable macroscopic properties. That this is possible is due to a long, elegant chain of scientific reasoning. The story, built up over the years from the life work of many thousands of individual scientists, is inspiring. As Walter has repeatedly demonstrated, it can also be used to inspire others.

Great scholars and teachers like Walter Kauzmann are extremely rare. They are critical for the scientific enterprise because they convey both the excitement and the rigor of science to many thousands of young people, providing the inspiration that is needed to guide the next generation of scientists.

One of my most treasured possessions is a gift from Walter: the first printing of *Thermodynamics and Statistics*, marked in his pen with 67 comments and corrections. On the frontispiece he wrote: 'To Bruce Alberts from Walter Kauzmann, in gratitude for the kind but inaccurate remarks made in May 1982 on the occasion of W.K.'s retirement.' When I retire, I hope that I shall be able to find some quiet place where I can carefully reread this book, and the companion volume that preceded it, *Kinetic Theory of Gases* [4]. As I point out elsewhere [2], the next generation of molecular and cell biologists will also need to master this material, if they are to be able to move our understanding of living cells to a higher level.

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