

Biophysicist in Profile



Clare Woodward

After growing up in a segregated southern city, *Clare Woodward* arrived in 1959 at Smith College, a place she describes as 'liberating'. "It was so refreshing to be surrounded by women who had intellectual aspirations," she explains, "and by faculty who encouraged us to achieve."

Smith provided a rich cultural mix that included teachers like *Leonard Baskin* and *Mary Ellen Chase*, and heated discussions of the writings of Smith alumnae *Betty Friedan* and *Sylvia Plath*. Just as important, Woodward met with social diversity and consciousness. The campus was abuzz with analyses of the Holocaust, and many drew parallels to civil rights issues. Woodward notes that "this was the first time I was introduced to social history and its relationship to the contemporary scene."

After her mother's death during her senior year, Woodward returned to her home in Houston and began graduate school at Rice University. The cultural shock couldn't have been more startling. "Universities and other institutions were polarized and changing fast," Woodward says, "and the overriding controversy was

integration." Rice was still segregated, and Woodward felt she had plunged into a "cauldron of divisiveness and racism." After three different advisors, Woodward finished her PhD degree in the lab of the department chair, *Clark Reed*, a proponent of integration who faced burning crosses in his front yard. Through Reed, Woodward met *Val Woodward*, who later become her husband, and who was also engaged in civil rights and the integration of Rice.

Woodward was born in Houston, Texas, a few days after the attack on Pearl Harbor. One of five children, she was encouraged by her mother, *Bernice Keating*, to embrace cultural and intellectual pursuits. Her mother, who had been the youngest graduate of Baylor College in Waco in the 1920s, taught Biology and English. Woodward's father, *Carl*, was an entrepreneur and salesman. Woodward describes her mother as having many of the same traits she later admired in her husband, namely, their "social outlook and respect for scholarship and teaching. They both cared about the disenfranchised," she says. "and saw themselves as agents of social change and social justice."

Colleague and friend *Mary Barkley*, of Case Western University, sees those traits in Clare as well. "Clare has incredibly insightful perspectives and good judgment," Barkley notes, "her integrity and courage, plus the patience of Job, make her a very effective change agent."

Woodward developed an interest in science and academic achievement early in life, an interest that was fostered in large part by her mother. Graduating from high school at age 17 — in a class of about 100, of which a small percentage went on to college — Woodward received

a partial scholarship to Smith College. Although she started as a pre-med major, she graduated with a degree in chemistry.

After completing her PhD at Rice, Clare married *Val Woodward*, a biology professor at Rice, and promptly moved to the University of Minnesota (UM) where Val had accepted a professorship. There, she worked without pay for a year and a half because of anti-nepotism policies. After completing a postdoc in chemistry, she took a non-tenure track position in the medical school at UM. In 1972, she became the first woman at that institution hired for a tenure track position. She remained in the Biological Sciences department at UM for her entire professional career. Although the tenure-track appointment of a woman was met with opposition by some older faculty in her department, the support from younger faculty was heartening.

Clare Woodward's research is in the area of hydrogen exchange and its relationship to protein fluctuation and folding, an interest she developed as a postdoc. She initially used a tritium exchange method, and in the mid-seventies switched to Nuclear Magnetic Resonance (NMR) to measure deuterium-hydrogen exchange at atomic level resolution.

Her research involves study of the kinetics of hydrogen-deuterium isotope exchange of backbone NH hydrogens in proteins. As Woodward describes it, "of particular interest are amide hydrogens that are buried in a folded protein, and that undergo slow isotope exchange with solvent hydrogens on the hour-to-day time scale at neutral pH and room temperature. Slow exchange immediately implies the existence of internal motions of the folded state that expose buried amide NH groups to solvent and thereby to isotope exchange. Although exchange is a result of protein internal motility, the hydrogen exchange experiment does not usually yield the frequency or amplitude of a motion, but rather a probability that

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a given NH will exchange with solvent hydrogens. This deceptively simple measurement of protein behavior opens a window on complex dynamical properties and associated biological functions, and monitors a subset of these. Woodward and her associates think that the internal fluctuations of folded proteins responsible for slow exchange of buried amides most likely involve rapid, small motions (tenths of angstroms) that occasionally allow transient access, or penetration, of solvent to buried regions of the protein.

Jannette Carey, Professor of Chemistry, Princeton University, characterizes other aspects of Woodward's research, "Based on her abundant and sound evidence collected by NMR, Clare proposed that faster amides exchange independently of the global unfolding of the protein, while, in the same experiment, the slowest amides usually mark secondary structure elements that exchange only by cooperative unfolding of the entire chain. Clare's proposal, known as the 'two process model', has become a founding concept in our current understanding of protein hydrogen exchange and folding."



Clare and Val Woodward met at Rice University during the socially turbulent 1960s.

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Woodward and her associates also conclude that their results and analyses indicate that the part of the protein that is least susceptible to exchange when the protein is folded is also the part to become organized first during folding. This is embodied in the hypothesis that the slow exchange core is the folding core, sometimes nicknamed last out, first in. The mutually packed elements of secondary structure that contain the slowest exchanging protons are the elements of secondary structure that are most likely to sample native configurations during folding.

Woodward's work has had far-reaching impact. *Bertrand Garcia-Moreno*, Professor of Biophysics at John Hopkins University, says that "the work in our laboratory (and in many others!) has been influenced significantly by some of the concepts that emerged from Clare's research on hydrogen exchange and protein dynamics and folding. Clare was one of the pioneers of hydrogen exchange studies with proteins by NMR. This was very exciting work at a very exciting time when protein chemists had to come to terms with the fact that proteins were highly dynamic molecules."

In addition to her mother and the support and encouragement of her husband, Woodward credits a number of others with having had a lasting impact on her science. Among them are *Rufus Lumry*, emeritus professor at the University of Minnesota and a Fellow of the Biophysical Society; the late *Gregorio Weber*, who was very influential in protein dynamics; and the late *Linderstrom-Lang* and his associate, *Aase Hvidt*. And

from afar, she was encouraged by the esteemed *John Edsall*, whom she refers to as a "Great Grandfather" of the field.

Have things changed since she first started science? "I think professional doors opened up somewhat for women and underrepresented minorities and then closed again", Woodward says. She has worked hard to ensure that diversity in science is fostered. "It's better for science to have diverse perspectives," Woodward notes, "the way a question is framed and the way data are interpreted, are significantly influenced by the researcher's overview of the field. When a scientific field is primarily a white, male dominated club, it is constrained by a uniform overview promulgated by a rigid hierarchy, and that's not good for science."

Woodward has won national and UM awards for her work in teaching and mentoring young people. In fact she says that she is most proud of the work she has done to help identify, mentor, encourage, coach, and open doors for younger people,

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women, and underrepresented minorities at the undergraduate and graduate level. A former undergraduate advisee of Clare's, *Valerie Copié*, Professor of Chemistry at Montana State University, notes that "I do not think I would ever have gone to graduate school, or obtained a PhD in chemistry at MIT, if not for the crucial role Clare played in my education and in my career."

Wayne Bolen, Professor of Structural Biology/Biophysical Chemistry, University of Texas Medical Branch, first met Clare when he joined the laboratory of Rufus Lumry in 1970. Bolen says that "Her enthusiasm for science is engaging and contagious, so she always has people

(Continued on page 26.)

(Continued from page 7.)

requesting time with her to discuss their work. Her passion for science and support of the careers of colleagues and young researchers carries an enduring legacy, along with the superb example she set for others in the Society." Garcia-Moreno also praises Woodward's commitment to young scientists. "Clare

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has always been very highly supportive of young scientists," he explains. "She played an active role in supporting and promoting the science and the professional development of many young biophysicists."

Woodward advises those starting out in biophysics to "try and understand everything there is to know about your scientific area, and then formulate an interesting question that can be feasibly probed by specified methodologies. You have to persuade your colleagues that your question is worthwhile, and that you have identified and acquired appropriate theoretical and/or experimental techniques to pursue the question. At the personal level, I have observed that those who organize their life to ensure relationships in which the career aspirations of both partners are mutually supported, are more likely to find science a joy, not a source of stress."

The Biophysical Society has been an important component of Woodward's professional career. Since her initial national meeting in 1970, Woodward says the Society is "where I first established contact with colleagues. This is most important, especially for women — having colleagues who truly examine your work, consider it deeply, and give you critical feedback." She

immediately began bringing her students and postdocs to the meetings as well, and says the Society has always been particularly "hospitable to young people and students." Woodward has served on many Society committees, and was President in 1997-1998, successfully overseeing a very difficult and tumultuous period in the Society's financial and governance structure.

Woodward and her husband now reside in Utah. Both are officially retired, although she maintains a formal affiliation with the University of Minnesota as Professor Emerita, which permits her to continue collaboration with Professor *George Branay*. She co-advises students and postdocs, mainly through telephone and email. "I was fortunate to get a research-teaching position when universities were first hiring women,"

Woodward says, "and to retire at a time when electronic communication has blossomed." In addition, she lectures and reviews papers for colleagues.

"Clare Woodward is a multidimensional person with many interests, and she knows how to have fun," explains Bolen. "She and her husband Val enjoy the great outdoors, living in the mountains of Utah, with frequent trips in their camper to the desert, the coast, and national parks. It has been my pleasure and good fortune to have them as friends."

"There is an essential unity of the humanities and sciences. I never felt they are dichotomous, but rather that they are intertwined in the life of the mind," Woodward says. "I feel fortunate to have had teachers and colleagues who know and appreciate both."



Photos: *Clare Woodward* and colleague *Ann Rougvie*, University of Minnesota, hiking in the northern Utah mountains (upper left). With former student *Natalia Carulla*, a biophysicist in Barcelona, Spain, in front of the Woodward cabin in northern Utah (upper right), and hiking in the northern Utah Mountains (bottom).