

In memoriam – Rainer Jaenicke



Rainer Jaenicke was a pioneer in the field of protein folding. He died on July 26, 2016 at the age of 85. His scientific work laid the groundwork for our present-day understanding of how oligomeric proteins fold, how they assemble into biologically active entities and how their reactions are steered kinetically. In an inspiring way, he combined high-level physical and chemical knowledge with an almost fatherly affection for proteins. This combination allowed him to unravel the complex interrelations between the processes of protein folding and oligomeric assembly.

Rainer studied chemistry at the University of Frankfurt (Germany) and obtained his doctoral degree in physical chemistry there. In the course of this early work, he developed an interest in the thermal denaturation of proteins and in the application of the analytical ultracentrifuge to investigate the behavior of proteins. As a postdoctoral fellow with Max A. Lauffer at the University of Pittsburgh, he focused on the mechanism of entropy-driven assembly of tobacco mosaic virus, and this work further shaped his interest of the complex interplay between protein folding and association. Soon after returning to Germany in 1970, he was recruited for the Chair for Physical Biochemistry at the newly founded university at Regensburg. There, within a short

time, he established a center recognized both nationally and internationally for protein research and in particular for protein folding. In his center, he provided space and support for young researchers, equivalent to assistant professors. Under his auspices they were free to develop their own scientific identities. He provided full support to them for all aspects of becoming mature scientists, but at the same time granted them full freedom in their scientific work - a role model for a senior scientist that was rather rare then in German science.

The productive folding of large oligomeric proteins is notoriously plagued by unwanted aggregation, and all groups working in this field undertook major efforts to find conditions under which this nasty side reaction could be suppressed. Rainer Jaenicke and his group were the first to ask why proteins have a tendency to aggregate. They recognized that nonspecific aggregation is the most important side reaction in protein folding and that the extent of aggregation is ultimately determined by the kinetic competition between aggregation and critical steps in productive folding. At that time, nonspecific aggregation was viewed as little more than an epiphenomenon of *in vitro* experiments, as protein aggregation *in vivo* was not yet a focus of interest. Rainer's publications were well ahead of the times, and are now recognized as classical papers on protein folding. This work in the 1970s foreshadowed the much later studies of protein aggregation in connection with inclusion body formation upon overexpression of recombinant protein aggregation, and of pathological protein aggregation associated with human diseases such as Alzheimer's and Parkinson's, and of the discovery of chaperones that suppress protein aggregation in the cell.

The folding and association of proteins constitute central biological processes of enormous complexity. In the early 1970s, the folding field was still dominated by studies of small well-

behaved model proteins, such as ribonuclease A, myoglobin and lysozyme, and few researchers dared to work with large proteins. In 1979, Rainer Jaenicke organized the first major conference on protein folding, and this landmark scientific meeting was extremely productive. For the first time, it brought together the experimentalists on protein folding with the then still small communities of structural biologists and theoreticians. This meeting focused the whole field and had a significant impact on the further development of the protein structure and folding community.

Rainer Jaenicke's seminal work initiated four lines of research that continue to be important in current protein science: (i) the development of procedures to renature recombinant proteins from inclusion bodies; (ii) the elucidation of the mechanisms of protein aggregation; (iii) the analysis of protein folding assisted by cellular folding helpers, such as molecular chaperones; and (iv) the forces stabilizing thermophilic proteins. Right after the discovery of hyperthermophilic organisms (in particular by his Regensburg colleague Karl-Otto Stetter), Rainer Jaenicke embarked on unraveling how these enormously robust proteins fold, why they are so stable against thermal unfolding, and why they often are inactive at room temperature.

Rainer Jaenicke contributed to the protein folding field not only by his research, but also by a series of classical review articles that served as comprehensive and reliable references for a whole generation of protein folders. He was a member of EMBO, of the German National Academy of Science - Leopoldina, awardee of the Max-Planck-Prize for Research, and he was a visiting scientist at leading institutions including the Institut Pasteur, the National Institutes of Health, Birkbeck College London, and the Universities in Cambridge, Zürich and Basel.

Rainer's achievements are all the more impressive when it is realized that he lacked primary school education. Born into a family with one Jewish parent just two years before the

establishment of the Third Reich, the Jaenickes were eventually confined in the Frankfurt Ghetto, where children were deprived of formal schooling. Though enduring hardships, the family avoided deportation to death camps, and Rainer was 14 when defeat of the Nazi regime allowed him to enroll in secondary school.

Rainer Jaenicke was both an eminent researcher and a superb teacher, devoted to his students and colleagues. He promoted protein science in Germany and elsewhere. As a generous and compassionate mentor he became a role model for a whole generation of scientists in basic and applied protein science. In his laboratory, he nurtured a large number of future prominent protein biochemists, among them Jim Bardwell, Rudi Glockshuber and Robert Seckler. Rainer was an avid musician, as well as a lover of the arts and classical literature. Once when listening to classical music with one of us, he identified by ear not only the composer (Haydn) but also the performers (the Beaux Arts Trio). In his dealing with colleagues, he exuded a gentle and humane spirit. We miss him and we will hold him in our memories.

Johannes Buchner, David Eisenberg, and Franz Schmid