Wolfgang Doster

About my scientific career

I studied physics at the Technical University in Stuttgart. My study group was mainly interested in theoretical physics. We admired the great laser theorist Herrmann Haken, who should have won the Nobel prize together with Prigogine. Life is not just. Later he created the field of "Synergetics", concerned with the origin of collective phenomena in nature. From microscopic reversibility to macroscopic irreversibility. He introduced the concept of "slaving" for the adiabatic elimination of fast variables: Slow variables slave the motion of fast variables, electrons follow the nuclei etc. Later Frauenfelder reused "slaving" as a catch-word to denote the solvent-viscosity dependence of protein motions. Here slow variables are controlled by fast solvent motions.

After finalizing my basic studies in physics in Stuttgart with the "Vordiplom", I continued at the newly founded university at Ulm with a special focus on polymers. W. Pechold developed his great meander model of polymer melts, which was later disproven. I could convince the laser theorist H. Risken ("the Fokker Planck Equation") to give a series of lectures on Irreversible Thermodynamics, which deeply impressed me. Risken didn't like the subject too much, he was more interested in irreversible statistical mechanics. I got a good overview of the relevance of molecular dynamics. These were the days, where Alder and Wainwright for the first time performed MD simulations of hard spheres. I wrote a theoretical Diplom thesis guided by the well-known NMR polymer scientist Rainer Kimmich on Monte Carlo simulations of the De Gennes defect model of polymer melts. In my simulation the defects would interact along the chain like hard sticks, which leads to anomalous diffusion. Later lateral interactions turned out to be more important.

After the Diplom in physics, I wanted to find out how to apply the polymer dynamics models of Flory to biomolecules. Also I was interested in collective phenomena in biological cells. I could get a phD position at the Max Planck Institut with Benno Hess in Dortmund. He was famous for his experiments with biochemical oscillations in yeast cells. My project was concerned however with protein folding and unfolding of multi-subunit enzymes using the new techniques of dynamic light scattering. I put together a Malvern photon correlation spectrometer. Initially each data point of the correlation function had to be written down by hand. Here I learned a lot about statistical processes, diffusion and correlation functions, which would be extremely useful with neutron scattering. I also learned a lot about protein preparation and aggregation. My thesis was concerned with the folding-unfolding transition of tetrameric proteins observed with several methods, activity, CD, UV and static and dynamic light scattering. This was the first folding-unfolding study of a multi-subunit enzyme observed DLS and was published in Biochemistry in 1980. It was ahead of its time.

Instead of going ahead to molecular biology, I made the big mistake to turn back to physics. Benno Hess had suggested a postdoc with the physicist Hans Frauenfelder, who had just published a T-dependent X-ray displacements study of myoglobin in Nature (1978). Most of it turned out be wrong later, specially the anharmonic potential analysis. But it was quite fun

to work with a group of phD students in Urbana, Lou Reinisch, Shyam Shamsunder, Sam Bowne and others, on low temperature dynamics of myoglobin.

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I learned how to use helium and flash photolysis on a log time base. First I got interested in the IR bands of myoglobin-bound CO. For such early FT-IR experiments we had to drive several hundred miles to Ohio, to the lab of Jim Alben. We discovered light-induced reactions of photolysed CO near 10 K. At one night an earthquake shocked the interferometer, which ruined our data.

Later I focused on the pH dependence and the protonation of the distal histidine of myoglobin and its effect on ligand binding, which was also published in Biochemistry. We also looked at a mutant without histidine, Hemoglobin Zürich. The protonation of the distal histidine became a major issue in later kinetic and mutation studies of heme proteins. As an independent project, I studied the CO binding to horse raddish peroxidase and the role of molecular tunneling, published in J.Mol. Biol.

In 1982 I got a second post doc position at the Technical University Munich in the amorphous metal group of Edgar Lüscher. Edgar was quite nice, but there was very little equipment for a biophysicist, I had to start from scratch, there was no support from any German biophysics group, for instance F. Parak. I started with an old dispersive IR spectrometer and a DSC1 to study the low temperature properties of protein hydration water. We introduced the concept of a glass transition from the IR spectra and calorimetry. We also performed time resolved Brilloin difference experiments with lysozyme solutions with an old ruby pulse laser (published in Biopolymers). At a Biophysics Conference in Bristol about 1987 I met Steve Cusack and we decided to perform inelastic neutron scattering experiments of hydrated proteins at low temperatures. The idea was to investigate the glass forming process on a faster times scale. At that time it was very difficult get support for experiments with biomolecules at sub-physiological temperatures.

The Institut Laue Langevin in Grenoble around 1988 was a great place to work with people with broad knowledge. The relevance of elastic neutron scattering to molecular motions I learned from Franz Fujara and W. Petry who studied liquid dynamics (glycerol, OTP) and the glass transition. This dynamic transition would show up as an anomalous increase in the linear temperature dependence of molecular displacements. Our data on hydrated proteins looked very similar to what other collegues measured for just solvents. We had the impression that before understanding protein dynamics, we had to cope with liquid dynamics. These were the great days, where in Munich mode coupling theory of the liquid glass transition was developed by Wolfgang Götze and his group. The theory predicts directly the neutron scattering spectra and their temperature dependence. In 1988 we first published a paper comparing myoglobin simulations with our neutron scattering experiments, a combined effort of Cusack, Smith and Martin Karplus. In 1989 we published a letter in Nature on the dynamical transition. We had developed our own ideas, related to the glass transition of hydration water coupled to protein motions. With these and other new experiments on a

home-made flash photolysis spectrometer I proposed new features to Frauenfelders conformational substate model. Never propose new ideas before you are well established.

Around 1989 I had established a unique biophysics group at the Technical University Munich, physics department which would combine home-made techniques of low temperature flash photolysis for ligand binding to heme proteins, frequency dependent calorimetry (glass transition) and dynamic neutron scattering (ultrafast molecular motions in proteins). The hard core of the group were several bright students like Marcus Settles (neutron scattering), Harald Leyser (calorimetry), Franz Demmel (IR), Frank Post and Thomas Kleinert (flash photolysis). Later Martin Diehl, M.S. Appavou and Ann Gaspar (neutron scattering, pressure) joined the group. With this combination, we could study the effect of solvent dynamics (temperature, viscosity and pressure) on bio-molecular function and structural dynamics. We derived two independent classes of protein motions, dependent and independent from the properties of the solvent. In particular the rigid active site was shielded from the exposure to a mobile solvent. External collaborations with S. Longeville in Paris would allow for the first time to observe the motions of hemoglobin inside blood cells. In the first decade after 2000 the focus was on pressure effects and the low temperature properties of protein hydration water. Our view was challenged by Frauenfelder and related workers. Part of this discussion is documented at the Web site. In particular, collegues from condensed matter dynamics became interested in hydration water. Stanley and Chen suggested a fragile-strong cross over around 220 K as an alternative structural explanation to the dynamical or glass transition. We could disprove this conjecture with dynamic neutron scattering experiments on a per-deuterated protein hydrated with H_2O published in Phys.Rev. Lett. (2010). To prove something in Science does not mean very much. Believe and conviction are often stronger. Officially I retired in 2013, but I left the Institut of Winfried Petry at the Physics Department of the TU in Munich in 2008 because of discrepancies and lacking support. That I created a new field from scratch and published many basic papers, which received some 4000 citations, did not promote my career very much. Instead I was considered by some collegues as a dangerous competitor, who had to be eliminated. Some of them were very active behind the scene and from 2001 on also with many un-reviewed papers in PNAS. However I received generous financial support by the German Government, which made possible many interesting experiments and the work of bright students. My personal summary is positive. Neutron scattering is a very expensive method with problematic side effects, which generates nuclear waste if performed with reactors. One of my postdocs came from Japan after the Fukushima accident. He had to be cleared from low but measurable levels of radioactivity after arriving in Germany. Thus, performing research with such a technique should be reduced to the absolutely necessary level at high scientific standards by aware and responsible scientists.