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Interview by Ute Deichmann with Jack Dunitz

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Jack Dunitz, FRS, studied chemistry in Glasgow, and then received research fellowships at the University of Oxford, at Caltech, at the NIH, and the Royal Institution in London, before he became professor of chemical crystallography at the ETH in Zurich in 1957. Since 1990 he has continued his research at the ETH as professor emeritus.

On the wall of his office are pictures of his scientific heroes: David Hume, Dorothy Crowfoot-Hodgkin, Spinoza, Albert Einstein, Max Perutz, and Linus Pauling.

Part I - On Gerhard Schmidt and his initiation of the Israeli-German collaboration in the sciences

UD: Can we first talk about Gerhard Schmidt and his crystallography and then about yourself and your work? You met Gerhard Schmidt in 1946 in Oxford, where you were a post-doctoral fellow, and he was…

JD: I was already a post-doctoral fellow, and Gerhard was still working on his doctorate though he was older than I, because his scientific studies had been interrupted by the fact that he was arrested with all other German citizens over 18 years old in 1940, sent to the Isle of Man, and then to Australia. Did you know about that? Well I'll give you my version. He was sent to Australia and thus disappeared from Oxford – he was an undergraduate at the time, and the professor of organic chemistry at Oxford, Sir Robert Robertson, was most upset that they had taken one of his best students away. He kicked up a row about it, and talked to the right people, and so Gerhard was sent back again from this camp, an "enemy aliens" camp as they were called. He came back to Oxford having lost maybe two years, that is why I was ahead of him.

There is a little anecdote which I want to tell you. It started in Oxford and ended about 15 years later in Rehovot: as a student Schmidt is attending a lecture by Sir Robert Robinson and Robinson is talking about organic chemistry and drawing molecules on the board. Now you probably know that carbon is tetravalent, a carbon atom makes 4 bonds. And Robinson wrote by accident 5 bonds in one of his atoms. Schmidt put up his hand. “Yes, yes Schmidt”. “Excuse me Professor, but you have a pentavalent carbon atom on the board.” So Robinson looks at the board, takes a duster, rubs out the offending bond, comes back, glares at Schmidt, and carries on his lecture. Many years later, Schmidt is meanwhile professor at the Weizmann Institute, Robinson has his Nobel Prize, and comes to the Weizmann Institute for some honorary doctorate or similar occasion. He is giving a lecture to a big auditorium. It was still the time of blackboards. Robinson draws a formula, and this time Schmidt, sitting in the front, much more confident now, puts up his hand and says, “excuse me, Sir Robert, but you have a pentavalent carbon… Robinson turns around and says, “Schmidt, you again!?”

So Schmidt was doing his Ph.D. with Dorothy Hodgkin when I arrived, and shortly after that - this is interesting for the future of the Weizmann Institute - a young lady called Margaret Roberts, who was a student at Somerville College, came. At Oxford, undergraduates had to do an undergraduate research project as part of their studies towards the end. Dorothy Hodgkin was fellow and science tutor at this College. So students from Somerville tended to do their research project in Dorothy Hodgkin’s laboratory, among them Margaret Roberts. She was put under the direction of Gerhard Schmidt to help him in his work. Margaret Roberts graduated then and later studied law. She married Dennis Thatcher and became Margaret Thatcher. Many years later, when she was Minister of Education, she was the first British cabinet minister to visit Israel. And where did she visit? She visited the Weizmann Institute and also Schmidt, who was then still alive. It was the mid 1960s. Margaret Thatcher had always a good relationship with him. So the connection which started in Oxford with Gerhard Schmidt influenced the rest of her career.

I became very friendly with Gerhard. He played the flute and used to practice in the evening in our office. We got on very well with each other and we stayed in contact until the end of his life. In 1948 we departed from Oxford in different

directions: I went to Caltech, he to the Weizmann Institute. He had a wife then called Anita and she was a convinced Zionist.

UD: That may answer my question. Why of all countries did he go to Israel? He was certainly not a Zionist, right?

JD: No. No. Anita was the Zionist. Sometime during 1947-48 they wanted somebody who would introduce crystal structure analysis at the Weizmann Institute. They asked Isidor Fankuchen from the Brooklyn Polytechnic, who was a member of the board, to find an appropriate person. Fankuchen offered this position to Gerhard: 'why don't you go and introduce X-ray analysis at the Weizmann Institute?' Gerhard himself was ambivalent about it. But his wife, Anita, was Feuer und Flamme. So they went to Israel in August-September 1948, shortly after the establishment of the State of Israel.

Living conditions in 1948 in Israel were still rather hard. And after a year or so, Anita could not stand it. She had been used to a reasonably comfortable life in suburban London and Oxford. She left Gerhard and went back to London, whereas Gerhard, although he had not been particularly enthusiastic about Israel, started to love life there. He loved the sort of Wild West atmosphere close to the desert. Beer Sheba at that time — I visited it for the first time in 1962 — was like a place in Wild West films. And he loved it. So he stayed on and built up his group at the Weizmann Institute.

And he was very successful, as I tried to describe in my article [Gerhard Schmidt (1919-1971) and the Road to Chemical Crystallography'], and had very good students. He also rose up in the establishment, becoming professor and head of the department of crystallography in 1956. I think it was during that decade, between 1950 and 1960, that there came from Germany the first Minerva fellowship.

UD: The Minerva Foundation was created only in the early 1960s. But the official collaboration was prepared by individual scientists already in the end-1950s. It was Gerhard who went to Germany to visit his father, whom he had not seen since he left Germany. His father, who was professor of chemistry in München, introduced him to several scientists in Heidelberg, in particular to Wolfgang Gentner, who was known to have been an anti-Nazi. Gerhard also

visited some chemists iin Heidelberg. You probably know about his father, or did he not talk about it?

JD: I know that his father had been professor of technical chemistry at München, and his father and his mother divorced. In 1933 already. And then Gerhard went to London.

UD: But first to Switzerland.

JD: Did he? Oh, I only knew that he went to St. Paul's school in London. So where was he in Switzerland?

UD: Leslie Leiserowitz said he was in Italian-speaking Switzerland, which is why he spoke Italian so fluently. In any case, they went to London as fast as possible.

JD: So the father stayed in Germany?

UD: Yes, and he was member of the Nazi party.

JD: Was he a member of the party for convenience or for conviction?

UD: I don't know for sure. In any case, to sign the Nazi principles – it means something, doesn't it? Some people say – and this is probably right – that he was not a Nazi by conviction. In addition, he had money transferred to his son in England. But for many years his son was very angry, to the effect that though the father urged him to visit him, he did not come to Germany until 1956. There his father introduced him to people who were not Nazis. And obviously Gerhard was also interested in German chemistry and chemical industry, which was not developed in Israel.

JD: I remember, when he came here sometime during the 1950s, he had visited one of the industrial Germans, who had a Nazi past. We were in a group with some of my colleagues. Gerhard referred to this Mr "X" - I can't remember who it was - and described him as a "Schwein". One of my colleagues said, 'Gerhard, you shouldn't call a person a 'Schwein''. This Schwein was somebody in Hoechst or another of those big German companies.

So when did Gerhard's father die?

UD: That I do not know.

JD: He was still professor after the war, wasn't he?

UD: Yes; he was denazified; that is why he could stay professor. He did not take on a political function or receive a high rank in the NSDAP. But he remained a party member until the end.

JD: Yes, it was a sad time. One of the people I knew slightly, one of the "goodies" as it were at that time, was von Laue. And von Laue kept a connection with Einstein, not only throughout the pre-war period, but also after it.

UD: After the war it was probably difficult because the Germans, most non-Nazis, too, did not want to face the past. Instead they felt misunderstood by the rest of the world. Von Laue, too, did not understand the situation.

JD: I think you are on a very interesting topic. So – Gerhard is now in the Weizmann Institute, and is rising up. He told me once that in one of those meetings where he was advocating collaboration with German scientists – the Germans were offering considerable financial help and instrumentation –one of the colleagues at the Weizmann Institute said that he was absolutely against this and if they accept aid from Germany he will leave. Gerhard told him, "Weizmann needs help from Germany more than it needs you", which is quite brutal.

UD: So you think it was mostly the financial aspect that motivated Gerhard to promote the collaboration?

JD: Well, Gerhard's aim, as I see it, was to win financial help for the Weizmann Institute and new instrumentation. The first actual collaboration that I came in contact with was in 1964 or 65. I visited the Weizmann Institute, and Gerhard said, 'Oh, by the way, we have two young Germans here from Heidelberg.' It was a weekend, and they had gone off somewhere on a tour. We also went on a tour to that place on the Dead Sea side of the Judean mountains with the famous spring, Ein Gedi. There we met these two young Germans., One was Hermann Irngartinger who went back to Heidelberg and the other was Carl Krueger who went to the MPI für Kohlenforschung in Mülheim. They were among the first people to work in the crystallography of organic compounds in Germany, where crystal structure analysis had been developed mainly in mineralogical institutes. After the war it was nearly non-existent as far as

organic chemistry was concerned, because the people who had been doing it before were mainly Jewish or half-Jewish. They had all left. Including Hermann Mark.

UD: Yes, Mark was one of the initiators. But some scientists with a good expertise in crystal structure analysis of organic compounds were taken to the United States by the Americans after the war.

JD: So there was nobody left.

UD: What about Walter Hoppe?

JD: Hoppe was not an organic chemist but a very good physicist. His main interest was electron diffraction and electron microscopy rather than structure determination of organic molecules. He was at ETH for a few years with Fritz Laves who was professor here when I arrived in 1957. Laves was regarded as one of the good Germans. After the war ended he had gone as a non-Nazi to be a professor in Chicago. After five or six years he came back here as professor of crystallography at the ETH. Hoppe worked with him here and went on to a professorship in München.

To come back to the two young German scientists at the Weizmann Institute: They were the beginnings of, you might say, organic crystallography in Germany. They were both very good scientists. Now they are both retired, of course. As far as I know, they are both still living.

Who was the first German to go to the Weizmann Institute?

UD: The physicist Lorenz Krüger; he is no longer alive. To return to Gerhard Schmidt: He was very eager to help the Germans. When Leslie Leiserowitz spent two years in Heidelberg, Gerhard went there every few months to see how things were going.

JD: Leslie was sent to Germany?

UD: He introduced the first computerized crystallography to Staab's laboratory. A question in this context – have you met Amos de Shalit at the Weizmann Institute?

JD: Probably, but I don't remember. The person whom I met in those early visits, whom I liked very much and got on with especially well, was Schneor Lifson. And Katzir. I knew both of them. When my connection with Aharon (Katzir) was terminated by his early death, I kept on the connection with (Ephraim) Katzir before, during, and after the time when he became president.

My first visit to the Weizmann Institute was in 1962. It was an interesting visit because David Ginsburg, Professor at the Technion in Haifa, who was a constant visitor here, invited Eschenmoser, Heilbronner, Zollinger and myself to a lecture tour in Israel. We spent three to four days at the Technion, three to four days at the Hebrew University, three or four days at the Weizmann Institute, and three or four days on an adventurous tour in the Negev. That was the first time that I'd actually been there – Gerhard used to visit us often, during the 1950s and early '60s - but this was my first visit to the Weizmann Institute. My second visit was 1965 or '66.

UD: You wrote '66.

JD: '66 maybe. And then … When did Esther come into the picture? Esther, his second wife?

UD: I don't know.

JD: Well I think that by 1970 there was already at least a strong relationship. She had been married before; she had two boys. She was very good for Gerhard. She was also a very strong personality. And she was with him when he died. In 1971 Gerhard had his last sad stay here at the ETH. By then his health condition had strongly deteriorated. Esther kept him on an iron discipline. You know, he was a big smoker and that probably was contributory to his lung cancer. Esther was originally in the biology department at Weizmann, and then when she retired it was archaeology - she had always had this as a hobby: She was very knowledgeable about digging sites all over Israel.

As I said, Gerhard's last visit to Zurich was in 1971 and it was tragic. He was very ill. He wanted to give some lectures and he had to give them sitting down; he could not stand up for more than a few minutes. He gave a few lectures here at ETH and a few at the university. Then he went to Basel. On the Saturday morning Edgar Heilbronner, his host in Basel, phoned: "Gerhard is doing very poorly. There's no point to him staying to give any more lectures here. He has

to go back. You can come to pick him up". So I drove over and brought him back. During that drive back to Zurich he was aware that he was very, very seriously ill. And that night, he died in his hotel in Zurich.

Part II - On the crystallography of Gerhard Schmidt and crystallography in general

UD: If you don't mind, I would like to turn to crystallography. In your article 'Gerhard Schmidt (1919-1971) and the Road to Chemical Crystallography' you wrote that by 1945 Oxford had become a stronghold of the crystallography of complex organic molecules with, for example cholesterol. You also wrote that Gerhard unsuccessfully tried to solve the structure of a still more complex molecule in his thesis.

JD: That is the one that Margaret Thatcher, nee Roberts assisted him with. Dorothy [Crowfoot] used to go in for investigating problems that were, at the time, technically almost impossible to solve. And Gerhard was given one of those: It was Gramicidin-S, an antibiotic. It was extremely difficult to crystallize and the crystals were very bad. And once you got an X-ray pattern, one did not really know what to do with it.

UD: It shows his strong personality that he didn't give up. But would it not have been wiser by his supervisor Crowfoot to leave these complex structures for the future when new technological tools would be available?

JD: Well, yes, this would have been my attitude as well. To illustrate this, I'll tell you a little anecdote, not about Gerhard, but about Dorothy. Shortly after I came to Oxford, in late 1946 or 1947, I received a phone call from somebody in Cambridge called Dr. Perutz. Dr. Perutz had learned of my existence through my supervisor, Professor J.M. Robertson in Glasgow, and he asked me if I would like to come to Cambridge and give a seminar. This was the first time anybody had ever invited me.

UD: Shortly after you came to Oxford, it was?

JD: I came to Oxford in 1946. I had just finished my Ph.D. So I get this telephone call if I will come and give a seminar in Cambridge, of all places. I said, 'yes, that's wonderful.' I went to Cambridge and met all those famous

people there, and Max Perutz explained to me what he was trying to do. He was going to make what were called Patterson projections of the haemoglobin crystal and from this determine the atomic structure. On the way back on the train to Oxford, I thought about what Max had told me and proved to myself that what Max was trying to do was impossible – it couldn't work.

When I got back to Oxford, Dorothy asked me how did I get on, and so forth, and I told her "wonderful". And she asked me what I thought about Max's plans, and I said, "well, I can show you that what he is trying to do won't work". I gave her my arguments, and she agreed with me and said, "yes, you're quite right. But what you haven't taken into account is that as the years go past, the technical possibilities are improving. And some time or other, the computing facilities and measurement possibilities will be orders of magnitude better than they are now. And when that happens, Max will be prepared for it." That was her attitude as well. They were laying down a kind of groundwork which, when the situation was ripe, would be likely to succeed. Like planting a seed which was going to take a very long time to flower. In Gerhard's case, he came at a stage when it was pretty hopeless to solve the gramicidin problem. Gerhard himself was in any case not basically interested in biological problems. For work in that direction at the Weizmann he engaged Wolfie Traub. There was a man there called Wolfie Traub?

UD: Yes, Wolfie Traub was at the department of Crystallography at Weizmann.

JD: Well, Wolfie Traub was a South African brought in by Gerhard to work on protein crystal structures. One of Traub's students is Ada Yonath. So Ada is a scientific granddaughter of Gerhard. Gerhard attracted also a number of very gifted scientists, such as Leslie Leiserowitz, Meir Lahav and Fred Hirshfeld — is the name still remembered?

UD: I know it from my conversation with Leslie.

JD: Fred Hirshfeld spent a sabbatical year here at ETH. A wonderful scientist, a great theoretician and a very, very deep thinker.

Then there was Frank Herbstein who became professor at the Technion, and Dubie Rabinovich who died rather young. Phillip Coppens was a Ph.D. student of Gerhard who then went and became professor at New York State University, Buffalo where he spent the rest of his career. These are all top people in

science. Coppens became president of the International Union of Crystallography. I had a special connection with Leslie and Meir Lahav, who invented a new way of determining the absolute configuration of enantiomers, of deciding which enantiomer is which. Their method confirmed the correctness of the assignment that had been made in 1950 on the basis of anomalous dispersion of X-rays by the Dutch crystallographer Johannes Bijvoet. .

Now shall I try to explain to you what Gerhard did.

UD: I would like to ask - given all the crystallography of organic molecules which was conducted in Oxford, Cambridge, and other places, it sounds at first surprising that you wrote that Gerhard's major contribution to science was his synthesis of crystallography and chemistry. Did you mean that he started the study of chemical reactions within crystals after the long period in which crystallography was only concerned with the structure analysis of molecules?

JD: Yes, that's it. Of course, by making it possible to determine the structure of molecules by X-ray diffraction the crystallographers saved the organic chemists a lot of trouble because until the mid-50's or so, the main work of organic chemists had been exactly that — to determine the structure of molecules, how the atoms were put together. You isolated some compound, as found in a plant for example, and carried out all sorts of chemical reactions until you could deduce its chemical structure.

UD: Are you talking about the three-dimensional structure, or just the…?

JD: Well the three-dimensional structure could then sometimes be inferred. But the critical bits had to be confirmed. For instance, the six-membered ring of benzene was believed to be planar by the chemists but it was only proven to be planar by crystallography. And similarly, that the six-member ring of cyclohexane is different was again shown by crystallography. The chemists were very, very clever in determining the spatial structure of molecules by doing chemical reactions but it took up a lot of time and energy. And there was sometimes an element of doubt about the correctness of the conclusions. Then, in Britain about 1940 and in other countries about 1950 onwards, gradually, this task of molecular structure determination was taken over by crystallography – it was much faster to do it that way. And more reliable. You did not have to infer anything; Look? There it is, there are the atoms. So the new method was much

used to determine molecular structures, but apart from that, it was not contributing much to the understanding of chemical reactivity, of how molecules actually come together in a chemical reaction. Now, Gerhard in his work on solid state – on topochemical reactions, as they call them in chemistry, showed that, for example, there was a certain…

It was known that in the solid state, when a crystal is exposed to light, the molecules sometimes dimerize, that is, a pair of molecules combine to form a dimer. Gerhard looked at the structures of crystals where the molecules dimerize under light and also at the structures of closely related crystals where the molecules did not dimerize. The reaction in question was the formation of a four-membered ring from two C=C double bonds in separate molecules. He found that if the two double bonds in the crystal are sufficiently close together and parallel, then light causes them to dimerize but if the double bonds are arranged in another manner then nothing happens. Gerhard was the first to explain this solid-state chemical reaction in terms of the exact arrangement of the atoms that is necessary for the two molecules to combine.

I personally was very impressed by this kind of work. And that's really what that book is about. But apart from that, Gerhard was educated as an organic chemist. He didn't start off as a crystallographer who then learned some organic chemistry. He was an organic chemist who learned some crystallography. If Gerhard had lived on, he would surely have been a candidate for the Nobel Prize for this work. I'm not saying he would have been awarded the prize, but he would certainly have been a candidate. It is interesting, isn't it, that two Israel Nobel Prizes have been concerned with crystallography.

UD: Yes, Ada Jonath and the other awarded to Dan Shechtman. Israel has quite a prominent tradition in crystallography.

I would like to ask something else. In the article on Schmidt (p.263) you made an interesting statement on the role of theory in crystallography. You wrote that with a background in chemistry, Gerhard knew that progress in his subject has come about more as the result of systematization (of whole series of related structures) than of theory. But isn't theory – or hypotheses – necessary to render the systematization meaningful?

JD: Yes, in chemistry ..., in theoretical physics it is probably the other way around. Theoretical physicists, you know, they're people like Steven Weinberg who have all these conceptual pictures with quarks and so forth - I think there theory drives experiment. People have been looking for 20 years for this thing called the Higgs Boson. The theoretical physicists said, "Oh it has to be, even if it is not known". Then the experimentalists go out and now they have found it.

What I'm trying to say is that in chemistry it is mostly the other way round.... very few new chemical concepts have come directly from theory. In the chemical world, there were some facts, and the facts had to be explained, so we made a theory. But it was not, "the theory predicts some facts which seem incredible, like anti-particles". Then the experimentalists go out and find them. Of course, there were also experimental physicists like Rutherford, who were making discoveries which radically changed physics. Radioactivity changed physics. But there are also many examples in physics where a theory predicted that something totally surprising must happen, so let's go and look for it. There's much less of this in chemistry. What I'm trying to say is that in chemistry, the facts drive the theory - you make theories to explain the known facts, rather than you make theories to predict new facts.

And again, in biology – Darwin spent 30 years collecting bits of evidence before he dared to make a theory of it.

UD: Yes, but when you look at molecular biology, hypotheses drive the experiments.

JD: Yes, but not towards anti-DNA made of anti-matter. Even there, the facts – the facts. When the double stranded structure of DNA became accepted it gave rise to a big problem: how do the strands come apart? Francis Crick would have said: 'Don't worry about that. People will find the way it's done; the strands must come apart and people will find out how it's done.' Biology is so complicated that the facts come before anybody has made a theory. Afterwards lovely theories are made. Mendel? Nobody had found how properties are inherited from one generation to the next. Then it came out: One black, one white, and two khaki. Mendel showed it was like that. From observations of this kind came the theory that there must be genes.

UD: Yes, you're absolutely right, but people also say that Mendel had some kind of theory in his head before conducting the experiments.

JD: I don't think so. Mendel made observations, very clever ones. He perhaps sometimes had an idea that things should go this way or that way but he never really had a proper theory.

UD: He had an idea of invisible elements behind the phenomena.

JD: But on the other hand, in physics it was different. Einstein made a theory that when light passes material objects it will bend. Crazy? But it was found to be the case.

Of course, there are many examples in physics where experiments led to a radical change of theory. But physics is almost the only area where it can go the other way round, where theory predicts something that nobody has ever dreamt of or believed possible. And when you go and look for it, then there it is.

For example, Dirac predicted anti-particles. He said his equations are also valid when the mass is negative. Negative mass? Absurd! But within a couple of years Carl Anderson had discovered anti-matter.

Part III on Jack Dunitz's scientific biography

UD: I would like to talk now about yourself and the crystallography of biologically relevant macromolecules. You studied chemistry in Glasgow, Oxford, Caltech, NIH, and then you came to the ETH. You are now called the leading expert in the crystallography of molecular structures. Why as a chemist, did you choose this field of research?

JD: You can find the answer in my autobiographical article 'La Primavera'. Just briefly: I was educated a chemist. I did not choose crystallography, but crystallography chose me. I thought of myself as a frustrated mathematician. I thought I was good at mathematics. See, in school I was the best in the class at mathematics; 50 boys, I was the best. But when I went to university and passed into the class of advanced mathematics, everybody in that class had been best in their school class, so now it was not best out of 50, but best out of 50 times 50 – two and half thousand – and then I realized that there are boys who are far

better than I was in mathematics. But I always had a mathematical sort of interest. And physical chemistry was somewhere there with a mathematical flavour to it.

So I studied chemistry at Glasgow University. This was during the war. When I graduated B.Sc. in physical chemistry, most of my colleagues went away to do – there was some secret research going on and they disappeared – now we know it was radar. So most of the boys I studied with went into radar research. But we had a new professor - John Monteath Robertson, returned to Glasgow University as professor in 1943 - and he needed people to work with him in crystallography. In those days one didn't have much choice. They said, "you, you, and you will go and work on the secret work, and you, you, and you will go and work with Professor Robertson". During the war you could not choose a supervisor or direction of research. They were chosen for you. So I came to Professor Robertson and to chemical crystallography.

During that time, I read articles in the area and learned about Dorothy Hodgkin's work, which I greatly admired, so I wrote to her and said 'can I come and work in your laboratory?' She said, "yes", so I went to work in her laboratory and (pointing to a photograph) after two years, this gentleman here came on a…

UD: Linus Pauling? Wasn't he at Caltech?

JD: Yes, but he was visiting professor at Oxford. He came in January 1948 and stayed for six months. Before he left he invited me to join his research group, an invitation that I could hardly refuse. In the late summer of that year I went to Caltech and stayed there three years.

UD: You went to Caltech to study with Pauling?

JD: Yes, to be in his research group. Actually, I didn't work directly very much with Pauling. I only got occasional words of wisdom from him. I worked mainly with Verner Schomaker. Then I went back to Oxford for a couple of years because I had left unfinished things. During this time in Oxford I got mixed up to a small extent with the people in Cambridge, Francis Crick and Jim Watson, who worked on the structure of DNA.

I ended up here at ETH, because the organic chemist Professor Leopold Ruzicka, who was going to retire in 1957, wanted to have a crystallographer

established in this group before he left. He had probably talked to Dorothy Hodgkin about this. The rumor is that he had offered the job to her, and that she said, 'I can't do it, because my husband cannot speak German. We have to stay at Oxford.' So they asked me instead. Does the name Leslie Orgel mean anything to you?

UD: Yes. I wanted to invite him to my symposium some years ago, but he had already just passed away.

JD: Well, after my first stay at Caltech, I had a very nice collaboration with him in Oxford around 1952. We wrote a joint paper, which was published in Nature, on the molecular structure determination of a new type of molecule and a new theoretical model [the fascinating collaboration is described in Jack Dunitz's autobiographical essay]. Leslie died five years ago and one of his students, Jerry Joyce and I have recently written the biographical memoir for the Royal Society; it is now being published. I can send you a copy. [Now published as J. D. Dunitz and G. F. Joyce, Biographical Memoirs of the Royal Society 2013, volume 59, 277-290]

UD: If is it possible to say - which of your contributions became most influential?

JD: My main work was in molecular structure research. On the whole, in science, I am a bit of an opportunist, I see a problem, I think I can solve it, so I become involved. I don't start off with the big unsolved problems of science.

I was involved with Leslie Orgel in the determination of the structure of bis-cyclopentadienyl iron — ferrocene — and the theory which accounted for the stability of this molecule and related molecules. With Verner Schomaker I determined the precise structure of cyclobutane and accounted for some of its unusual properties. When I came to Zurich, I worked for a time on what was called the conformations of medium rings. And we worked on the structure of ionophores, antibiotics that make the bacterial membrane transparent to ions - essentially they make holes in the membrane so that ions can pass backwards and forwards.

There was also my work on chemical reaction paths. I had the idea that, when molecules come together in crystals, this process can sometimes be regarded as the incipient stage of a chemical reaction. a chemical reaction that does not go to completion. If one looks at crystal structures, one can observe how

molecules approach each other. Similar to Gerhard, you see. And this approach was developed at about the same time. So the knowledge of how things are in crystals can give you an idea of the geometrical relationships that are necessary for bond formation. This is very much the case in hydrogen bonding. A hydrogen bond, for me, is an incipient proton transfer. A hydrogen bond is the beginning of a reaction in which a proton jumps from one atom to another.

Then there were some isolated papers, including theoretical ones, which were not part of big research programmes. But they gave the answer to questions that had worried me and obviously not worried other people, otherwise they would have been answered already. As an example; what would happen to a hydrogen molecule if the charge of the proton did not equal the charge of the electron? What if the charge of the proton and the electron were slightly different? Say the charge of the proton was a little bit bigger than the charge of the electron, would the hydrogen molecule be more stable or less stable? Most people thought it would be less stable. But I thought the opposite, I thought that it should be more stable! This is just an example of my excursions into theoretical chemistry or physics…

UD: Did you approach them experimentally or theoretically?

JD: Theoretically. You can't answer that problem experimentally because you can't make protons with a charge of +1.1.

UD: I've read a citation of you from 1990: "Diversity in ways of scientific thinking is nowhere greater than in the contrast between the search for abstract unifying laws of nature and the awareness of the infinite complexity of the real world."

JD: Did I write this?

UD: Yes, it was published at the homepage of the collection of your papers at the archives of Oregon State University.

JD: Really? Well that sounds very good! I did not know I had written that.

UD: But you would agree with it?

JD: Say it again.

UD: “Diversity in ways of scientific thinking is nowhere greater than in the contrast between the search for abstract unifying laws of nature, and the awareness of the infinite complexity of the real world.”

JD: Well, I think it is good, yes.

UD: I’m glad you agree with yourself!

JD: Yes, I have no idea why or where I wrote that. Well, at Oregon they have everything - they have all my correspondence. I’ll ask them some time. I agree with it, and I think it is very well said.

UD: My question is still, isn’t it the aim of chemistry also to find unifying principles underlying the complexity?

JD: Yes, of course. And here chemistry is - continuing what we said before - in this intermediate area between quantum physics, let’s say, and biology. An enzyme is the result of five billion years of evolution. And the present structure of an enzyme depends on history, not on any principles. It has to follow certain rules, but it is not derivable from those rules. It is a result of history.

UD: But aren’t physical objects, too, the result of history?

JD: Yes, but the physical world also is existing elsewhere, and we can take samples of it. We have outer space at 2.3 K or whatever the temperature is supposed to be out there. I think there’s still a lot of physics still to be discovered. I don’t want to say that the theory of relativity is wrong, of course it is not wrong. And I don’t want to say that quantum theory is wrong. But I think they are both incomplete versions of the universe. Nobody understands why the value of the gravitational constant g is what it is? It is there to 15 significant figures or so. Why is it that value? Nobody knows.

When I was the dean of faculty, 25 years ago, I had to go to all the Ph.D. exams in chemistry. If there were good candidates, I would ask them questions like this: you know there are all these physical constants, you can look then up in a book, so what would the world be like if Planck’s constant were 10% bigger than it is? And good students would give you an answer to that. Nobody knows why Planck’s constant is what it is. And all those other numbers. Nobody has any idea why these numbers are what they are. Are they really independent or do they depend on one another? These seem to me to be fundamental problems of

physics which hardly anybody at present is interested in. Perhaps I'm mistaken. Perhaps they have already been answered. But I think not.

So what was your question there? Do I think that physics....?.

UD: The question was, doesn't also chemistry aim at finding unifying principles underlying the complexity? In biology, when you go to the molecular level you find many unifying elements underlying the macroscopic complexity. For example ATP, DNA and the genetic code ...

JD: Yes, but that is history. That is evolution, that says that we all have a common precursor. Once a mechanism is invented to do something in biological evolution you cannot change it. There may be a better way to do it, but then you have to change everything. And so once life started and life evolved to a certain degree, what came after that is what is possible given history, but not what must be. Consider problems like the development of plants. In the pre or early biotic world, oxygen was toxic. And when plants came and started to produce oxygen, it more or less destroyed all other forms of life. A few survivors of that destruction developed into organisms that needed oxygen. Nearly all the history of what was happening before this has disappeared. Well, there are a few bacteria for which oxygen is not necessary – for which oxygen is toxic. They live deep, deep down in the soil where there's no oxygen. Or deep down in the bottom of the ocean where there's no oxygen. But we could have had another history. So I think that in biology there are no first principles except evolution. Darwin is one of the cleverest who ever came along.

UD: I would like to talk a bit about Linus Pauling. I have read your wonderful biographical memoir on Pauling. Do you know why Pauling became interested in biologically relevant macromolecules in the 1930s?

JD: It was purely a question of money. The Rockefeller Foundation decided that it was going to stop or reduce its investment in chemistry and physics and was going to increase spending in biology. They told Pauling that he was only going to get funded if he does something with biological relevance. His first project was to work on blood. It was known for centuries that arterial and venous blood have different colors and other different properties. A doctor knows immediately

whether it is venous or arterial blood. Pauling showed that haemoglobin changes its magnetic properties when it becomes oxygenated.

UD: And he has the 1936 paper with Mirsky on protein structures.

JD: Yes, that is an important paper. A two-stage model of protein denaturation. It could be that Mirsky had suggested this problem to Pauling, and then the paper came out as a result. And then a few years after the alpha-helix paper came that strange odd-man-out paper with Robert Corey on the DNA structure, perhaps Pauling's biggest blunder. It may be interesting to know whether he knew about Chargaff's ratios. I knew about them in 1952 through Sydney Brenner. We discussed them then. If we had been smart enough, we could have said, 'Chargaff's ratios mean that there is a polymer in which adenine only interacts with thymine.' That is why it is 1:1. And therefore, a message written on one strand has a complementary message on the other. We did not know the structure, but we could have said: Chargaff's ratios are an important clue to how genetic information is transferred.

UD: But Pauling did not consider this.

JD: It is believed that Pauling and Chargaff once went on the same boat across the Atlantic. In those days you went by boat. Pauling could not stand Chargaff. Therefore, he did not listen to him.

UD: Is this true? I mean is it true that they went on the same...

JD: Possibly. A recent book by Mario Livio deals with this topic. Livio is an astrophysicist with an interest in the history of science. The book is called Brilliant Blunders. Livio took five great scientists who made, in the course of their work, one big mistake. The five are Darwin - Darwin's mistake is that although he knew of Mendel's experiments, he took no notice of them...

UD: Yes, but he was unable to do it. His approach was too different.

JD: The second is Lord Kelvin and his theory about the cooling of the earth, where he was several orders of magnitude wrong. According to Livio this was not only because he neglected radioactivity, but also because he neglected convection and considered only conduction.

The third is Fred Hoyle with his insistence on the stationary universe. The fourth is Pauling, with his three-stranded DNA. And the fifth is Einstein, with his insistence on the cosmological constant. It is quite a nice book.

I talked with Pauling about it. He told me, 'Jack, don't be afraid to make a mistake. Mistakes don't do any harm in science, because there are thousands of people out there who are only waiting to correct other people. So don't worry; if you make a mistake, it will do no harm. It can't do any harm. But if you're too cautious, you might miss a good idea.'

UD: Yes, he followed this rule, didn't he? He made quite a number of mistakes.

JD: Another time he said, "look, if you never make a mistake, you're working in a field that is too easy for you. And that is a big mistake." Livio reports that Chargaff had told Pauling about his results, and that Pauling, because of his impatience with Chargaff as a person, did not even listen to him.

UD: Chargaff was an Austrian Jewish intellectual. And Pauling was a man from Oregon. He was more down to earth. Chargaff annoyed many people because he was an intellectual snob. And because he was so bitter.

Chargaff himself may not have understood his ratios. He thought these base couples were on one strand.

JD: Yes, and also he was tremendously pompous. I once heard a talk by him. He was off-putting and with his Austrian classical education contemptuous of most of his colleagues because they had never read Socrates in the original. If you have never read Socrates or Plato, how can you possibly talk about science? He wrote this book, which is full of…

UD: Heraclitean Fire

JD: Yes.

UD: His books were quite popular in Germany.

JD: Did he write the books, then, in German?

UD: I don't know in which language he wrote them. It is well possible that he wrote some of his books in German. But he also – I mean, he spoke 10 languages.

To come back to Pauling, I thought that the facts that he had worked on hydrogen bonds and that hydrogen bonds were so important for the spatial structure of proteins, caused him to turn to biologically relevant molecules.

JD: In my Pauling memoir I mention that, around 1936, Pauling wrote an essay on the structure of proteins and it was very heavily hydrogen bond. In the same year Bernal was also concerned with the hydrogen bond. He determined the structure of ice, which is held together by hydrogen bonds. But in Bernal's essay about the same time on proteins, hydrogen bonds are not mentioned.

Part IV on general issues

JD: (pointing to pictures at the wall): These are my scientific heroes! This (Pauling) is obvious. This one (Max Perutz) is obvious. There's Dorothy. Do you know who the next one is – that one? Do you recognize him?

UD: No.

JD: This is David Hume. And this is Spinoza!

UD: Ah! Really, Spinoza?

JD: So it is believed – yes.

A very interesting book on Spinoza was published a couple of years ago. It is known that Leibniz visited Spinoza. When he was a young man, about 25 years old, he went to Den Haag in order to talk to Spinoza. Six months later Spinoza died. We have no record of what happened, except that in his diaries, Leibniz referred often to this meeting with Spinoza. And recently, Matthew Stewart, a young American philosopher has written a book to try to reconstruct the conversation between Leibniz and Spinoza, in 1685 or something like that. And we have no way, of course, of checking that.

I'll ask you now a question which has stumped me about this history of science in the 20th century. I know personally about a dozen great scientists who were boys in Vienna in 1938. And in 1938 they emigrated either to England or to America, and they became hotshot scientists. I know about ten. Perutz is one.

Then there is the man on memory - Eric Kandel. A Nobel for the establishment of the molecular basis of memory; Carl Djerassi, Hermann Bondi, Karl Popper...

UD: Hermann Mark?

JD: Mark was already of an older generation. He could have been the father of any of these. Thomas Gold – a physicist at Cornell. Victor Weisskopf. I think if I go through my list I've got about 12 of them.

Then Martin Karplus – Harvard Professor (since our conversation joint winner of the Nobel Prize in Chemistry 2013). A dozen or so people, who include several Nobel Prizes, were all schoolboys in Vienna in the 1930s. Was there something about the educational system in Vienna in the 30s which made a background for the development of all these, or had it something to do with the psychological pressure of being shot out from one environment – by the way, all of them came from relatively comfortable backgrounds in Vienna. And they attended the best schools in Vienna. In comparison, if I try to count the number of great scientists of that age who came into exile from Germany or from Italy it cannot compare with this collection from Vienna. I can't think of any other city that produced so many absolutely top scientists of about the same age at the same time.

UD: I studied the forced immigration of people who were already established. And among them, you have this really exceptional group of German-Jewish biochemists, many of whom received Nobel Prizes either in Germany or afterwards.

JD: And one who didn't – Warburg. He stayed.

UD: But got a Nobel Prize.

JD: Yes, but he stayed Germany.

UD: Yes, he did not emigrate. He didn't consider himself a Jew.

JD: He didn't, but the Nazis did.

UD: He was actually 'half Jewish', but the Nazis made him a 'quarter Jew'. He stayed in Berlin and had big problems at the end. But he survived. The others - Otto Meyerhof, Carl Neuberg, and, a little younger, Fritz Lipmann, Rudolf

Schoenheimer, Hans Krebs, Konrad Bloch, and others – great biochemists. They came from different German towns or cities, though. But they all received a great school and university education. Another phenomenon, more similar to Vienna, is the great scientists from Budapest.

JD: Oh yes, that was the earlier generation. Wigner, Szilard, …

UD: Polanyi.

JD: I think the Vienna crowd is even more concentrated. The Budapest generation – they were between the first war and the second.

UD: Yes, but it is a similar phenomenon. I don't know to what extent it is related to schools, but certainly it is related to families. To very noble families – I mean, families which gave the children a wonderful education and cultural background. I think that this educational ideal was shared by these families in Vienna too. There were also good scientists before.

JD: - Yes. The history of science is a wonderful area.

UD: Yes, it is.

JD: And the present students are so ignorant about this. They learn organic chemistry but they have no idea of what organic chemistry was in 1850, or in 1900, or even 1950, or how ideas have developed. I was lucky. In Glasgow, we had a course – not an important course - but we had a series of lectures on the history of chemistry, with some emphasis on the history of chemistry in Glasgow. Nevertheless, we were aware of history, starting off with ancient Egypt and making beer there and so on. And then, throughout the ages, how our science developed into what it is today. This, as far as I can see, is absolutely absent in the present education of students.

UD: My last question is, which role does crystallography play in modern molecular biology.

JD: Well, it is the principal sources of structural informal at the molecular level. There are now probably several thousand new protein crystal structures determined every year. The protein database contains 50,000 structures.

We have a very good group here at the ETH in biomolecular structure, one of the best anywhere.

You must keep in mind that what took Perutz 15 years can now be done in a week or less. If you are not too fussy, it might even be done in a day or so. Since then the size and complexity of biological systems that can be crystallized have increased enormously; in addition to soluble proteins there are membrane proteins and complex systems like ribosomes and viruses, little biological machines that carry out biological processes. Also the intensity of X-radiation available from synchrotron sources is orders of magnitude greater than the most powerful X-ray tubes available in former times. Then there is the replacement of photographic film by digital imaging devices that can count single photons — the same change that has made film cameras practically obsolete in everyday life. There is also the enormous improvement in the ease of looking at the new structures: computer graphics were unknown in those early days. As a result of all this, there are now so many protein crystal structures that a new one attracts little attention from non-specialists. It will rarely hit the headlines. When I went to the Royal Institution in 1956, there were only about five proteins that had ever been crystallized. Apart from hemoglobin, there were myoglobin, chymotrypsin, pepsin, ribonuclease, lysozyme, ... very few.

And as with small molecule crystallography – what I did in the three years of my doctoral work you now can do in a day, less even If you work hard.

UD: Is there any work done on the crystallography of the cell protoplasma?

JD: I don't know how crystalline you can make it. But one of the most striking things achieved is the ribosome. Ribosome! – when Ada Yonath started her project, everyone said, 'it's impossible'.

UD: And she crystallized it?

JD: Yes. In fact, the person who developed the techniques for obtaining good crystals of such complex bio-structures at cryo-temperatures – his contribution is often passed over – was Hakon Hope, a Norwegian scientist who was professor at the University of California Davis. Hope developed the techniques of rapidly cooling biomolecular systems to preserve their structural integrity. As sabbatical visitor at the Weizmann Institute, Hope applied this method to

Yonath's crystalline specimens. The trick was to cool very fast. It was the general belief that "you've got to do it very slowly" but Hope claimed the opposite: "you've got to do it as fast as possible." And he was right. Ada was one of the first people who followed his approach, which is now accepted as standard.

The future is going to be with smaller and smaller crystals, because protein crystallographers use a synchrotron to irradiate their samples.

Well, you can ask Ada herself about the future of bio-crystallography.

UD: Yes, I should do that.

Thank you very much for this fascinating conversation.