

# Disputed X-ray data unresolved

*The letters from Hendrickson and Paradies on the two preceding pages raise doubts about the authenticity of a series of published papers. Here is a guide for readers.*

THE resignation as of mid-April 1983 of Professor Hasko Paradies from his chair of biology at the Free University of Berlin comes a year after the university had started an investigation into charges of scientific fraud. Paradies leaves behind him a string of disputed publications and the question of how he survived so long in a career that was first challenged in 1970.

The university's investigation was begun on the basis of a dossier compiled by Dr Wayne Hendrickson of the Naval Research Laboratory in Washington DC, whose doubts about some of Paradies's published work are expressed on page 195 followed by a reply from Paradies. If true, the charges are dismaying.

It was a seminar given by Paradies in March 1982 at the Naval Research Laboratory before he spent a sabbatical there that spurred Hendrickson into action. But he was already aware of doubts about Paradies stemming from his departure from King's College in 1970.

Paradies had been given space at King's College, London, to determine the crystallographic structure of transfer RNA, the family of molecules that carry specific amino acids to their site of assembly into proteins according to the instructions of the genetic code.

Crystallographic structure determination cannot begin without a crystal and Paradies first came to prominence with his claim, at a meeting in 1967, to have produced crystals of transfer RNA. It also brought him into contact with the Medical Research Council's Laboratory of Molecular Biology in Cambridge, where Brian F. C. Clark was also trying to crystallize transfer RNA and from which Kenneth Holmes was about to join the Max Planck Institute for Medical Research in Heidelberg.

Holmes offered Paradies, then aged 26 and with an MD from the University of Munster, a job. He was first to go to the University of Uppsala to learn about crystallography from Bror Strandberg and then to come to Heidelberg. It was from Uppsala that Paradies's first paper on the crystallization of transfer RNA appeared in 1968. It was also from Uppsala that Paradies visited Brian Clark's laboratory, which was finding difficulty in reproducing Paradies's protocol for the crystallization.

Paradies arrived without his own crystals, claiming they had been lost in an accident on the ferry from Germany to Sweden and, according to Clark, failed to produce any more crystals in his month or

so at Cambridge. Shortly thereafter Clark succeeded in getting crystals by a modification of the Paradies protocol. Clark published his results in *Nature* (219, 1222; 1968) and generously, it may be thought, made Paradies a co-author on the paper for having stimulated the protocol that was eventually successful.

Paradies continued his studies at Uppsala from where (but some time after he had left) he published the first diffraction pattern from a transfer RNA crystal (the 1970 *Nature* paper that is the focus of Hendrickson's accusation of "deliberate misrepresentation").

From Uppsala, Paradies went to Heidelberg, as planned, but stayed there only a few months, to appear at King's College London asking for space to pursue his work. Watson Fuller recalls that Paradies came at the end of 1969 with good qualifications and a reputation as immensely energetic and somewhat eccentric.

By September 1970, Paradies was claiming in King's College to have more good crystals of transfer RNA and excellent X-ray diffraction patterns from them. By chance David Blow paid a visit to the King's College laboratory and had a chance to look at Paradies's diffraction patterns. Blow was certain there was something odd about what he was shown and asked Paradies some questions that led him to produce other prints from his files. It was then that Blow recognized one of the prints as from his own crystallographic studies of chymotrypsin. Blow recalls that Paradies admitted as much when challenged. Paradies says that it was Watson Fuller, not Blow, who raised the issue of chymotrypsin.

After that incident, Paradies was advised to leave King's College. He returned to his native Germany but was back in October saying that he had been offered a job by Heinz-Gunter Wittman in his Max Planck Institute in Berlin. That news led to a letter from Watson Fuller to Wittman in December 1970 in which the full circumstances of Paradies's departure from King's College were explained.

Nevertheless, Paradies got his job with Wittman and there he stayed until 1974 when he obtained his tenured post of professor of biology at the Free University of Berlin. Dr H. Ibbeken, now vice-president of the university, who was in charge of the investigation earlier this year, says Paradies's appointment followed regular procedures, which would have included

obtaining Wittman's opinion.

Paradies published one paper from Wittman's laboratory on crystallized ribosomes — and three from his university claiming the crystallization of important enzymes. It is Hendrickson's contention that all of these papers are dubious and that the earlier papers on transfer RNA crystals are fraudulent.

His suspicions aroused early last year, Hendrickson carefully examined all of Paradies's publications. As detailed on page 195, he decided to determine the parameters of the crystal whose X-ray diffraction pattern was published in Paradies's 1970 paper in *Nature*. When Dr Gary Gilliland was asked, without being told why, to match the calculated parameters to those of proteins in a library of data he was compiling, he came back with the answer — carbonic anhydrase B, one of the proteins studied at Uppsala when Paradies was there.

Paradies, in his reply on page 196, denies the charges. The crux of his reply is that Hendrickson's recalculation of the crystal parameters is meaningless because "the magnification, not indicated in Fig. 2, is different in the horizontal and vertical planes". That, says Hendrickson, is not altogether impossible but is very hard to believe. David Blow goes further. "Paradies's explanation is not credible", he says, "because the curves which appear as parts of circles in the figure would have come out as ellipses" had there been different magnifications.

Presumably the Free University of Berlin had come to similarly trending conclusions when its investigations led it early this year to seek to remove Paradies from his post. That entailed ministerial approval which eventually was forthcoming. Shortly afterwards Paradies resigned but, he said this week, for reasons completely unconnected with the investigations. The university's letter accepting the resignation makes no mention of the investigation, he added.

In his wake are a cluster of disputed publications analysed by Dr Hendrickson and another cluster, some of which arise from periods when Paradies visited Cornell University from Berlin, that will no doubt now be scrutinized. But there remains some degree of praise from all those involved in early attempts to crystallize transfer RNA. Whether or not Paradies ever himself produced such crystals, they say, his protocol for doing so included at least one innovative step.

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