

Experiment Report Form

The double page inside this form is to be filled in by all users or groups of users who have had access to beam time for measurements at the ESRF.

Once completed, the report should be submitted electronically to the User Office using the **Electronic Report Submission Application:**

<http://193.49.43.2:8080/smis/servlet/UserUtils?start>

Reports supporting requests for additional beam time

Reports can now be submitted independently of new proposals – it is necessary simply to indicate the number of the report(s) supporting a new proposal on the proposal form.

The Review Committees reserve the right to reject new proposals from groups who have not reported on the use of beam time allocated previously.

Reports on experiments relating to long term projects

Proposers awarded beam time for a long term project are required to submit an interim report at the end of each year, irrespective of the number of shifts of beam time they have used.

Published papers

All users must give proper credit to ESRF staff members and proper mention to ESRF facilities which were essential for the results described in any ensuing publication. Further, they are obliged to send to the Joint ESRF/ ILL library the complete reference and the abstract of all papers appearing in print, and resulting from the use of the ESRF.

Should you wish to make more general comments on the experiment, please note them on the User Evaluation Form, and send both the Report and the Evaluation Form to the User Office.

Deadlines for submission of Experimental Reports

- 1st March for experiments carried out up until June of the previous year;
- 1st September for experiments carried out up until January of the same year.

Instructions for preparing your Report

- fill in a separate form for each project or series of measurements.
- type your report, in English.
- include the reference number of the proposal to which the report refers.
- make sure that the text, tables and figures fit into the space available.
- if your work is published or is in press, you may prefer to paste in the abstract, and add full reference details. If the abstract is in a language other than English, please include an English translation.



	Experiment title: X-ray Crystallographic Studies in the Phenylalanine to Adrenaline Pathway	Experiment number: 01-02-611
Beamline: BM01A	Date of experiment: from: 05.02.03 to: 07.02.03	Date of report: 31.08.04
Shifts: 6	Local contact(s): Dr. Jon Are Beukes	<i>Received at ESRF:</i>
Names and affiliations of applicants (* indicates experimentalists): Edward Hough*, Ole Andreas Andersen*, Ronny Helland*, Ellen Wang* Department of Chemistry University of Tromsø N-9037 Tromsø Norway		

Report:

After many data collections mainly at BM01, but occasionally on other ESRF beamlines, this project has now been completed.

The data collections lead to refined X-ray structures which made a major contribution to our understanding of the reaction mechanism and some aspects of the regulation of the highly important human phenylalanine hydroxylase.

The first step in this chain of events was the solution of the structure of the enzyme in its active Fe(II) form. This was followed by solution of the structure of a complex with the active reduced co-factor tetrahydrobiopterin¹.

Further experiments lead to determination of the structures of the PAH-Fe(II)/BH₄ complex and PAH complexed with the substrate Thienylalanine² and with L-norleucine^{2,3}.

These structures formed the central part of Ole Andreas Andersen's PhD thesis⁴.

References

- 1) O A Andersen, T. Flatmark & E. Hough (2001) High resolution crystal structures of the catalytic domain of human phenylalanine hydroxylase in its catalytically active Fe(II) and binary complex with Tetrahydrobiopterin. *J.Mol.Biol.* **314**, 279-291.
- 2) O A Andersen, T. Flatmark & E. Hough (2002). Crystal structure of the ternary complex of the catalytic domain of human phenylalanine hydroxylase with Tetrahydrobiopterin and 3-(2-Thienyl)-L-alanine and its implication for the mechanism of catalysis and substrate recognition. *J.Mol.Biol.* **320**, 1095-1108.

- 3) O A Andersen, A.J.Stokka, T. Flatmark & E. Hough (2003). 2.0Å resolution crystal structures of the ternary complexes of human phenylalanine hydroxylase with Tetrahydrobiopterin and 3-(2-Thienyl)-L-alanine or L-norleucine: Substrate specificity and molecular motions related to substrate binding. *J.Mol.Biol.* **333**, 747-757.
- 4) Ole Andreas Andersen (2003) Crystallographic and biochemical studies to elucidate the reaction mechanism and regulatory properties of human phenylalanine hydroxylase. PhD thesis, Department of Chemistry, Faculty of Science, University of Tromsø, Norway.

