EUROPEAN SYNCHROTRON RADIATION FACILITY

INSTALLATION EUROPEENNE DE RAYONNEMENT SYNCHROTRON

ESRF

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 via the User Portal:

https://wwws.esrf.fr/misapps/SMISWebClient/protected/welcome.do

Reports supporting requests for additional beam time

Reports can 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.

ESRF	**Experiment title:** Structural Studies of Signal Sequence Binding to SRP	**Experiment number**: MX-1557
Beamline: ID 14-4	**Date of experiment**: from: 10-Jul-2013, 17.00 to: 11-Jul-2013, 08.00	**Date of report**: 09-Oct-2013
Shifts: 2	**Local contact(s)**: MCCARTHY Andrew	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

SAUER-ERIKSSON Elisabeth

* HAINZL Tobias

* BEGUM Afshan

Report:

The main aim of this proposal was the structural characterization of SRP-signal sequence complexes. The Signal Recognition Particle (SRP) is a universally conserved protein-RNA complex which enables the co-translational membrane targeting of proteins. We have collected over ten data sets of an SRP-signal sequence complex which diffracted to 3.0 Ä (space group P21212, cell: 112, 122, 91, 90, 90, 90). We have now solved this structure using molecular replacement (current R-factor is 24 %, and R-free 27 %). Our aim is now to improve these crystals to diffract to higher resolution. We are doing this, using post-crystallization methods. A better resolution in this case is important to place crucial amino acid sequences undoubtedly in the electron density.

Other aims of this proposal were the structural characterization of: Transthyretin (TTR)-drug complexes. Mutations in the TTR gene cause transthyretin amyloidosis (ATTR), which is caused by the misfolding of protein monomers derived from the tetrameric protein. We have collected more than five data sets of TTR bound to different drugs. All of these drugs show high antitoxic activity in cell toxicity assays. These TTR-drug co-crystals diffracted to 1.5 Ä with one TTR-drug co-crystal even better than 1.1 Ä. All TTR-drug structures have now been solved and a manuscript is currently in preparation.

Two datasets were collected from the signalling domain of the transcriptional regulatory protein CpxR from *E.coli*. CpxR is a member of the two-component regulatory system CpxA/CpxR. This system combats a variety of extracytoplasmic protein-mediated toxicities. These crystals diffracted to 3,2 – 3,5 Ä resolution. We are currently trying to improve these crystals by modifying crystallization conditions.

Small crystals of the promoter region for the RNA dependent RNA polymerase in the Dengue RNA genome diffracted poorly and no data sets were collected. Dengue virus is a leading cause of serious illness and death

among children in Asian and Latin American countries. The Dengue virus belongs to the (+) RNA Flavivirus family which includes other viruses causing life threatening diseases such as West Nile virus, tick-borne encephalitis virus and yellow fever virus. We are currently trying to improve these crystals by modifying crystallization conditions and modifying the RNA constructs.