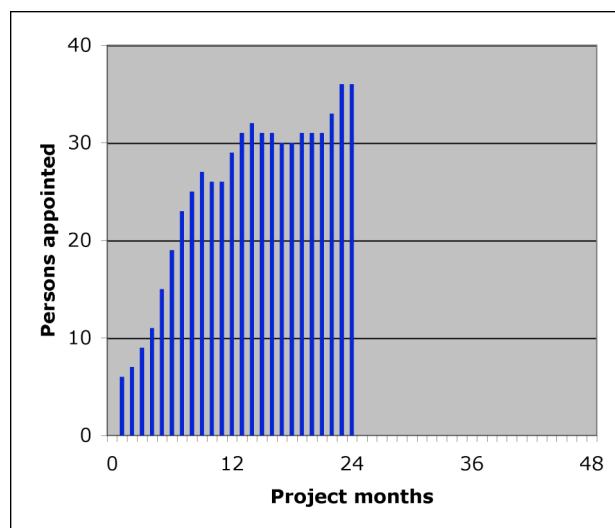


Executive Summary

The BIOXHIT project was launched on January 1st, 2004 with the aim of providing new effective tools for understanding complex biological processes at the molecular level. Within its projected lifetime of four years, the BIOXHIT Partners set out to develop, assemble and deliver an integrated platform for high-throughput structure determination using X-ray crystallography with synchrotron radiation. BIOXHIT is bringing together scientists from all European synchrotrons and leading software developers in both academic and industrial groups in a timely and unprecedented joint effort. The challenges arising from the complexity of the project and the inter-dependence of its research tasks are addressed by an efficient management structure. The BIOXHIT developments span the whole range of components required to produce an efficient high-throughput “pipeline” linking the crystallisation of a protein to the delivery of its completed 3D-structure. This pipeline will operate with minimal user intervention due to its integrated logistics. Once deployed and tested, it will be fully accessible to the wider life sciences research community through remote access facilities and an extensive program of training and dissemination at both synchrotron facilities and at satellite centres, which forms an essential part of the project.

The official start date of the project was January 1st, 2004. However, its real launch followed the BIOXHIT kick-off meeting that was held in Hamburg in April 2004. The first Annual Meeting was held in Barcelona on December 1-4, 2004 as part of an EU Joint Meeting for projects in Structural Genomics and Proteomics. After some delay in hiring during the first year, the number of the EC-funded appointments has now reached the expected level, see the Figure on the right. Overall within the first two years of the project 209 researchers, of which 36 are funded by the project, have been working on BIOXHIT goals at the various Partners' institutions.



The scale of the project as well as the requirements for reporting to the EC (task progress reports, milestones, deliverables, personnel, etc.) make it virtually impossible to distill all the scientific achievements and breakthroughs that happened during the first two years of the project into a short executive summary. For all details, the reader may advance to page 12, where the progress in all 115 scientific tasks that were active in year 2 is reported in detail. Here, just a few examples of the many BIOXHIT highlights are mentioned. One is the development of a new type of sensitive and extremely configurable X-ray fluorescence detector, optimised for easy integration into highly automated and cramped crystallography endstations. This detector has been jointly developed by BIOXHIT and an SME and has now become commercially available. Another one is the development in the direction of smart data collection with the use of multi-axes systems, which in the end will make diffraction data collection completely automatic and render even very small anomalous signals measurable. The third example comprises the autoSHARP and Auto-Rickshaw software pipelines for automated structure determination, which are emerging from the project. These pipelines enable the synchrotron beamline user to assess the quality of the collected data while the crystal is still at or near the beamline and decide on the spot whether a change in data collection strategy is required or not. This will undoubtedly lead to a much more efficient use of synchrotron beam time and crystalline samples. These and other scientific highlights will be presented in detail at the 2nd BIOXHIT Annual Meeting in January 2006.

Table 1. BIOXHIT Partners and their institutions.

Partner Role*	Partner No in Annex 1	Partner No in CPFs	Partner name	Partner short name	Country	Date enter project	Date exit project
CO	1A	1	EMBL Hamburg	EMBL-HH	DE	1	48
CR	1B	4	EMBL Grenoble	EMBL-GR	FR	1	48
CR	1C	7	EBI Hinxton	EMBL-EBI	UK	1	48
CR	2	2	ESRF Grenoble	ESRF	FR	1	48
CR	3	3	SRS/CCLRC Daresbury	CCLRC(SRS)	UK	1	48
CR	4	5	SLS Villigen	PSI	CH	1	48
CR	5	6	Global Phasing Ltd. Cambridge	GPHL	UK	1	48
CR	6	8	NKI Amsterdam	NKI	NL	1	48
CR	7	9	ELETTRA Trieste	ELETTRA	IT	1	48
CR	8	10	University of York	UOY	UK	1	48
CR	9	11	PSF Berlin	FUB	DE	1	48
CR	10	12	CCP4/CCLRC Daresbury	CCLRC-CCP4	UK	1	48
CR	11	13	AFMB Université Aix-Marseilles	UNIV-MRS	FR	1	48
CR	12	15	University of Göttingen	UNIGOE	DE	1	48
CR	13	17	SOLEIL Saclay	SOLEIL	FR	1	48
CR	14	18	IFOM Milano	FIRC-IFOM	IT	1	48
CR	15	20	MAXLAB-Lund University	MAXLAB	SE	1	48
CR	16	21	University of Copenhagen	UKBH	DK	1	48
CR	17	24	DIAMOND Chilton	DIAMOND	UK	1	48
CR	18	25	LLS Barcelona	LLS	ES	1	48
CR	19	26	HASYLAB/DESY Hamburg	DESY	DE	1	48
CR	20	27	EMBLEM	EMBLEM	DE	1	48
TP	1A	16	Max-Planck Group Hamburg	MPG-ASMB	DE	1	48
TP	2	14	IBS Grenoble	IBS	FR	1	48
TP	2	19	MRC-LMB Cambridge	MRC-LMB	UK	1	48
TP	11	22	LEBS-CNRS Gif-sur-Yvette	LEBS-CNRS	FR	1	48
TP	12	23	IBM Barcelona CSIC	IBM	ES	1	48
CR**	21	28	University of Vienna	UNIVIE	AUT	13	48

* CO = Coordinator, CR = Contractor, TP = third party

** From this document onwards the Partner University of Vienna is given number 21

Table 2. Overview of the status of the BIOXHIT activities given in the 13-30 months implementation plan.

Section	Work packages	Tasks	Milestones (months 13-30)	Milestones achieved by month 24	Deliverables (months 13-30)	Deliverables scheduled by month 24	Deliverables achieved by month 24
1-7	25	115	60	33	155	80	62

BIOXHIT is well on schedule, despite the initial delay in hiring in the first year of the project, Table 2. 60 milestones and 155 deliverables were planned for months 13-30. About half of them were due by month 24 and over 80 % of these have been achieved during the second year. The remainder will be during the third year. The success of the project is a consequence of the efficient monitoring of Partners' activities. However it also reflects the fact that many Partners mobilised resources, which were not funded from BIOXHIT.

Table 3a. Microsymposium on Structural Genomics (invited lectures of external speakers) and scientific BIOXHIT highlights presented during the second annual project meeting in Grenoble (January 2006).

Lecture no.	Lecture title	Scientist and Partner number of main author (email address)
L-01	Welcome to the ESRF and Introduction to BIOXHIT	Sine Larsen, Partner 16 (sine@ccs.ki.ku.dk)
L-02	Structural Genomics in FP6 and beyond	Josefina Enfedaque, European Commission (invited speaker)
L-03	Structural Genomics in the US from the JCSG perspective	Ian Wilson, Centre for Structural Genomics (invited speaker and member of SAB)
L-04	<i>In Silico</i> Prediction Based on Homology Modelling and Energy Calculations	Luis Serrano, EMBL Heidelberg (invited speaker, representative of 3D-Repertoire)
L-05	Structural Proteomics in Europe	Dave Stuart, The Wellcome Trust Centre for Human Genetics (invited speaker, representative of SPINE)
L-06	Progress with DNA and crystal centring	Andrew Leslie, MRC – Third Party (andrew@mrc-lmb.cam.ac.uk)
L-07	Transmissive XBPMS and an XRF detector optimised for Protein Crystallography	Martin Fuchs, Partner 9 (fuchs@bessy.de)
L-08	The EU BIOXHIT test crystal project	Ina Dix, Partner 12 (inadix@shelx.uni-ac.gwdg.de)
L-09	Report on TID Centres	Sine Larsen, Partner 16 (sine@ccs.ki.ku.dk)
L-10	A mini Kappa goniometer head for routine crystal reorientation	Sandor Brockhauser, Partner 1B (brockhauser@embl-grenoble.fr)
L-11	The Auto-Rickshaw system - validation of the X-ray experiment at the synchrotron beamline	Santosh Panjikar, Partner 1A (panikar@embl-hamburg.de)
L-12	Crystallisation technologies in BIOXHIT: What, why, where and how?	Anastassis Perrakis, Partner 6 (a.perrakis@nki.nl)
L-13	Predicting Radiation Damage	Gleb Bourenkov, MPG-ASMB Third Party (gleb@mpghdb.desy.de)
L-14	Section 5: Data Bases and Networking	Kim Henrick, Partner 1C (henrick@ebi.ac.uk)

Table 3b. BIOXHIT posters presented during the second annual project meeting in Grenoble (January 2006).

Poster no.	Poster title	Scientist and Partner number of main author (email address)
P-01	General BIOXHIT Poster	Victor Lamzin, Partner 1A (victor@embl-hamburg.de)
P-02	BIOXHIT Workpackage 5.1: Towards a Unified Data-Exchange Schema	Avi Naim, Partner 1C (naima@ebi.ac.uk)
P-03	The e-HTPX project for remote operation	Colin Nave, Partner 3 (c.nave@dl.ac.uk)
P-04	Coordinating crystallisation research and infrastructures in BIOXHIT	Patrick Celie, Partner 6, (p.celie@nki.nl)
P-05	Laboratory Information Management System for the BBSRC SPoRT Initiative	Petr Troshin, Partner 3, (p.v.troshin@dl.ac.uk)

P-06	Towards crystallisation PIMS-LIMS: a crystallisation experiment viewing and annotation interface	Diederick de Vries, Partner 6 (d.d.vries@nki.nl)
P-07	An application for automated optimisation of initial crystallisation conditions	Tahia BenHaj Abdellatif, IBS – Third Party (tahia.ben-haj-abdellatif@ibs.fr)
P-08	Determination of protein secondary structure from the Wilson plot	Andrey Bogomolov, Partner 1A (andrey.bogomolov@embl-hamburg.de)
P-09	Crystallisation drop analysis with a synchrotron X-ray beam	Jeremy Ohana, IBS – Third Party (Jeremy.ohana@ibs.fr)
P-10	Progress in BIOXHIT WP 5.2: Data Management for PX Structure Determination	Peter Briggs, Partner 10 (p.j.briggs@ccp4.ac.uk)
P-11	BIOXHIT website and database	Binoy Mathew, Partner 1A (binoy@embl-hamburg.de)
P-12	Status of the EMBL-Hamburg BW7B Sample Changer Control System	Uwe Ristau, Partner 1A (ristau@embl-hamburg.de)
P-13	How to avoid premature decay of your macromolecular crystal - a chemist's approach to combat physical reality	Brice Kauffmann, Partner 1A (brice@embl-hamburg.de)
P-14	Automated Molecular Replacement	Fei Long, Partner 8 (fei@ysbl.york.ac.uk)
P-15	Automated crystal reorientation	Florent Cipriani, Partner 1B (cipriani@embl.fr)
P-16	The Auto-Rickshaw system - validation of the X-ray experiment at the synchrotron beamline	Santosh Panjekar, Partner 1A (panjekar@embl-hamburg.de)
P-17	The EU BIOXHIT test crystal project	Ina Dix, Partner 12 (inadix@shelx.uni-ac.gwdg.de)
P-18	XREC: Automated Crystal Recognition Software (BIOXHIT tasks 1.2.6 and 3.2.1)	Babu Pothineni, Partner 1A (babu@embl-hamburg.de)
P-20	Artificial Intelligence for fault isolation on synchrotron beamlines	Olga Rudenko, Partner 13, (olga.rudenko@synchrotron-soleil.fr)
P-21	Algorithms for extending partial structures in ARP/warp	Krista Joosten, Partner 6 (k.joosten@nki.nl)
P-22	SNOW: An NCS-aware sequence docking, side chain fitting and refinement module in ARP/warp	Serge Cohen, Partner 6 (s.cohen@nki.nl)
P-23	Online Monitoring of UV/Vis Spectral Changes in Cryocooled Crystals	John McGeehan, Partner 1B (john.mcgeehan@embl-grenoble.fr)
P-24	The Poznan Training, Implementation and Dissemination (TID) Centre	Wojciech Rypniewski TID Centre Poznan, (wojtekr@ibch.poznan.pl)
P-25	Facility and method development in high-throughput crystallisation	Jochen Müller-Dieckmann, Partner 1A (jochenmd@embl-hamburg.de)

Scientific highlights were presented at the 2nd Annual Meeting in Grenoble (France) not only as lectures within the BIOXHIT-specific sessions, but also as posters directed at a general audience, Tables 3a and 3b. This demonstrates that many BIOXHIT tasks are well advanced and ready for a wider dissemination to the scientific public. It also portrays the close cooperation of BIOXHIT with related EU-projects. The presentations and posters are available to the Partners via the BIOXHIT website.

Fourteen BIOXHIT workshops or ad-hoc meetings on specific scientific topics have been organised during the second year of the project, Table 4. They represented activities from all scientific sections as well as the first training activities organised by the BIOXHIT TID centres. Five workshops were held jointly with related EU (SPINE and 3D-Repertoire) and UK-funded projects (PIMS, eHTPX, DNA, CCP4, CCPN), which are related to a number of BIOXHIT tasks. All of the workshops were well attended and provided a forum for fruitful interactions. A notable feature of the overall pattern of activities is the unprecedented degree of collaboration between groups of scientists associated with various European synchrotrons. The establishment of close and productive concertation between the staff at synchrotron beamlines, and of a spirit of collaboration in the pursuit of common solutions to common challenges has been installed and is fundamental to the success of the project.

Table 4. BIOXHIT workshops and ad-hoc meetings held during the second year.

No.	Workshop title	Date, location and attendees
1	Section 1 meeting	28 th January 2005, Amsterdam, The Netherlands, Section 1 contributors, 10 participants
2	Ad-hoc meeting on collaborations within Task 2.1.2	4 th February 2005, ESRF, Grenoble, France, 8 participants
3	BIOXHIT/eHTPX/CCP4 Workshop on "Automation standards and frameworks: from data reduction to structure"	9 th –11 th February, Cambridge, UK, 40 participants (http://www.ebi.ac.uk/msd-srv/docs/bioxhit05_1.html)
4	Meeting on AME-proposal for PSD-XBPM at BESSY	24 th February 2005, BESSY, Berlin, Germany, 12 participants
5	Adhoc DNA/BIOXHIT/CCPN discussion meeting	1 st -2 nd March 2005, Cambridge, UK, 4 participants (http://icarus.embl-hamburg.de/bioxhit/bioXHITDNAMarchMeeting.jsp)
6	PIMS, BIOXHIT, EMBL Joint Meeting	4 th March 2005, Amsterdam, The Netherlands, 9 participants (http://www.ebi.ac.uk/msd-srv/docs/pims1.html)
7	DNA Developers Meeting/ Kappa Workgroup Meeting	3 rd -6 th May 2005, EMBL Hamburg, Germany, 24 participants (http://icarus.embl-hamburg.de/bioxhit/bioXHITPastWorkshops.jsp)
8	The Joint SPINE/BIOXHIT Workshop on Imaging Systems in Crystallography	1 st -2 nd June 2005, Oxford, UK, 45 participants
9	BIOXHIT XPBM Workshop	6 th -7 th October 2005, Bessy, Berlin, Germany. 22 participants (http://www.psf.bessy.de/xbpmws2005/)
10	Workshop on Database Requirements for CCP4 Projects	17 th October 2005, University of York, UK, 16 participants (http://www.ccp4.ac.uk/peter/workshop/DBS17Oct2005/)
11	Section 3 dissemination meeting	23 rd -24 th November, CCLRC/ SRS, Daresbury, UK, 50 participants (http://www.srs.ac.uk/meetings/bioxhit3/index.htm)
12	1 st TID workshop on Biocrystallography using synchrotron radiation	28 th November–1 st December 2005, TID Centre Poznan, Poland, 24 participants, (http://www.man.poznan.pl/CBB/TID/)
13	2 nd TID workshop on Biocrystallography using synchrotron radiation	5 th -8 th December 2005, TID Centre Poznan, Poland, 23 participants, (http://www.man.poznan.pl/CBB/TID/)
14	BIOXHIT/ SPINE/ 3D-Repertoire Workshop on HTP macromolecular crystallisation	14 th -16 th December 2005, NKI, Amsterdam, The Netherlands, 45 participants (http://xtal.nki.nl/HTCrystal/)

Dissemination of both the objectives and the results of BIOXHIT has been an important activity in the second year. Over 80 lectures have been presented by BIOXHIT Partners on various occasions. 29 BIOXHIT posters have been presented at conferences, and 11 articles referring to the project tasks have been published. The latter include publications in scientific peer-reviewed journals as well as short announcements on topics of more general interest in newsletters, such as EMBL *et cetera*. Further dissemination activities include the regular updating of the official project web site www.bioxhit.org and the distribution of the BIOXHIT brochure at the EC organised conference on "Communicating European Science 2005" in Brussels (Belgium), November 13-15, 2005.

Two BIOXHIT Training, Implementation and Dissemination (TID) centres have been established: one in Oulu (Finland), <http://www.biochem oulu.fi/BIOXHITWEB>, and one in Poznan (Poland), <http://www.man.poznan.pl/CBB/TID>. These two centres are building up their facilities using the seed funds provided by BIOXHIT. The facilities are capable of disseminating BIOXHIT results to the wider scientific community in their own countries. The TID centre in Poznan held 2 workshops on Biocrystallography using synchrotron radiation in November and December 2005, which attracted participants from several European countries. The Polish TID will hold two more workshops in 2006 and 2007. The TID Centre in Oulu will hold its first workshop in summer 2007.

Two Project Steering Committee (PSC) meetings were held March and in October 2005. The next PSC meeting is scheduled for January 2006 in conjunction with the 2nd BIOXHIT Annual Meeting.