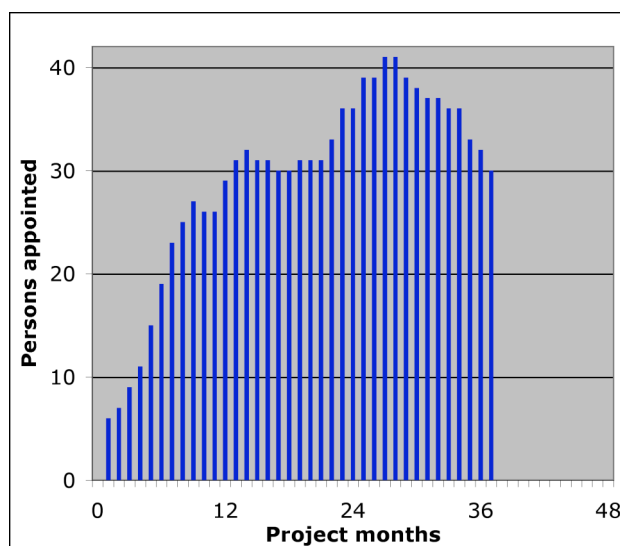


0. Executive Summary

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 launch of the project followed the BIOXHIT kick-off meeting held in Hamburg in April 2004. The 1st Annual Project Meeting was held in Barcelona on December 1-4, 2004 as part of an EU Joint Meeting for projects in Structural Genomics and Proteomics. The 2nd Annual Project Meeting was held at the ESRF premises in Grenoble, France, on January 18-19, 2006. After some delay in hiring during the first year, the number of the EC-funded appointments has reached the expected level, see the Figure on the right. Within the first three years of the project over 200 researchers, with 57 funded by the project, have been working on BIOXHIT goals at the various Partners' institutions. By the end of the year 3 the project has provided over 90 EC-funded person-years.



Appointments in BIOXHIT

In this short executive summary we are not attempting to distil all the scientific achievements and breakthroughs that occurred during the three years of the project. For all details, the reader may advance to page 16, where the progress in all 118 scientific tasks that were active in year 3 is reported in detail. Here, just a few examples of the many BIOXHIT highlights are mentioned. One is the development of a novel desktop crystallisation system based on free interface diffusion. In contrast to the commercially available expensive Fluidigm system, the new crystalliser is cheap, easy-to-operate and could be set up in any small or medium-scale laboratory. The other example is the new version of the DNA software where several new features have been introduced in order to get closer to what can be called a *real data collection pipeline*. This is already installed at several beamlines across Europe. The third scientific highlight achieved during the reporting period is the prediction of the effects of radiation damage on the quality of the experimental data within the software BEST. Based on the information contained in a few initial diffraction images, the optimal data collection strategy can be designed and proposed to either a user or an automated data collection system. This has already led to the successful acquisition of a number of diffraction data sets with significantly improved quality and information content. Last but not least is the development of mini-kappa goniometry for synchrotron end-stations. The impact that this will have on data quality can hardly be overestimated. Mini-kappa goniometry has already been successfully used during SAD data collections for several data sets measured from the samples in different orientation, hence for different crystal X-ray beam absorption configurations. These and other scientific highlights will be presented in detail at the 3rd BIOXHIT annual meeting in February 2007.

Table 1. BIOXHIT Partners and their institutions.

Partner Role ¹⁾	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 ²⁾	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 ²⁾	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 ²⁾	11	22	LEBS-CNRS Gif-sur-Yvette	LEBS-CNRS	FR	1	48
TP	12	23	IBM Barcelona CSIC	IBM	ES	1	48
CR ³⁾	21	28	University of Vienna	UNIVIE	AUT	13	48
TP ⁴⁾	22	29	University of Oxford	UOX	UK		

¹⁾ CO = Coordinator, CR = Contractor, TP = third party.

²⁾ AFMB, LEBS-CNRS and IFOM are in the process of leaving the project.

³⁾ From this document onwards, UNIVIE is referred to as Partner number 21.

⁴⁾ UOX is in the process of joining the project.

Table 2. Overview of the status of the BIOXHIT activities described in the 25-42 months implementation plan.

Sections	Work packages	Tasks	Milestones (months 25-42)	Milestones achieved by month 36	by	Deliverables (months 25-42)	Deliverables achieved by month 36	by
1-7	24	118	40	15		156	71	

BIOXHIT is well on schedule, despite the initial delay in hiring in the first year of the project, Table 2. 37 milestones and 156 deliverables were planned for months 25-42. About 80% of them were due by month 36 and about half have been achieved during the third year. The delay is generally modest and most of the these deliverables are well on course with the delay being mainly due to availability of suitable personnel. 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.

Prior to the 3rd BIOXHIT Annual Meeting a one-day conference on "*The Role of Structures in Biology – Past, Present and Future*" will be held at the premises of Project Partner 17, Diamond on 19th February 2007. International experts in the field of the use of synchrotron radiation in biological research will present their point of view as well as representatives from major funding agencies and the industrial sector. The invited speakers and the title of their lectures are listed in Table 3a.

The conference will be followed by the 3rd BIOXHIT Annual Meeting, 20th – 21st February 2007. BIOXHIT highlights from each scientific Section including lectures from two of the BIOXHIT TID centres will be presented, Table 3b. This will be accompanied by poster presentations from the BIOXHIT community as well as some external guests, Table 3c. The topics will cover crystallisation technology, synchrotron beamlines, beamline end-stations and data collection, data processing and structure determination, databases and networking, training, implementation and dissemination. Out of the anticipated 140 participants more than 40 are interested scientists from outside the BIOXHIT project and company representatives - five of these will be presenting posters. In addition, a British company, Molecular Dimensions Ltd., Suffolk, UK, requested and was granted to organise an exhibition stand at the conference. The presentations and poster abstracts are available electronically via the BIOXHIT website.

Table 3a. Conference on "*The Role of Structures in Biology – Past, Present and Future*" (invited lectures of external speakers), February 19th, Didcot, UK

Lecture no.	Lecture title	Invited speaker (email address)
L-01	Structural Biology facing the new challenges in the biology of the 21st century	Luis Serrano (luis.serrano@crg.es)
L-02	High throughput structural genomics and its applications to structural biology	Ian Wilson, Scripps Institute (iwilson@scripps.edu)
L-03	Structural studies on cell cycle regulatory proteins	Louise Johnson, Diamond (louise.johnson@diamond.ac.uk)
L-04	What made high resolution structures of the ribosome possible?	Venki Ramakrishnan, MRC (ramak@mrc-lmb.cam.ac.uk)
L-05	FESP – Forum for European Structural Proteomics	Gunter Schneider, Karolinska Institute, (Gunter.Schneider@ki.se)
L-06	Structural Proteomics in the EU: gathering the fruits of a collaborative effort	Josefina Enfedaque, EC (Enfedaque@ec.europa.eu)
L-07	Protein Structure Initiative: Progress and Plans	John Norvell, NIH (NORVELLJ@nigms.nih.gov)
L-08	Impact of the BIOXHIT project on structural biology	Sine Larsen, University of Copenhagen (sine@ccs.ki.ku.dk)
L-09	Better, faster, cheaper – The industrialist view	Dave Brown, Pfizer (david.g.brown@pfizer.com)
L-10	The big, the bad and the beautiful; structural virology at synchrotrons	David Stuart, University of Oxford (dave@strubi.ox.ac.uk)
L-11	Structural Genomics as a route to understanding TB Biology	Edward Baker, University of Auckland (ted.baker@auckland.ac.nz)

Table 3b Scientific BIOXHIT highlights that will be presented during the 3rd annual Project meeting in Didcot, UK (19th to 21st February 2007).

Lecture no.	Lecture title	Scientist and Partner number of main author (email address)
L-01-BIOXHIT	Section 1 overview	Anastassis Perrakis, Partner 6 (a.perraksi@nki.nl)
L-02-BIOXHIT	FIC crystalliser	Jochen Müller-Dieckmann, Partner 1A (jochenmd@embl-hamburg.de)
L-03-BIOXHIT	Current crystallisation methods, drops chips and capillaries	Patrick Celie, Partner 6 (p.celie@nki.nl)
L-04-BIOXHIT	Section 5 overview	Kim Henrick, Partner 1C (Henrick@ebi.ac.uk)
L-05-BIOXHIT	There and back again: A Crystal's tale (or how to get your crystal data to the synchrotron and data back again!)	Ian Berry, Partner 8 (ian@strubi.ox.ac.uk)
L-06-BIOXHIT	User experience with the data collection pipeline	Johan Turkenburg, Partner 8 (jpt@ysbl.york.ac.uk)
L-07-BIOXHIT	Section 2 overview	Sean McSweeney, Partner 2 (seanmcs@esrf.fr)
L-08-BIOXHIT	Vibration measurement and analysis on PROXIMA 1 and some implications for micro-focus MX Beamlines	Andrew Thompson, Partner 13 (andrew.thompson@synchrotron-soleil.fr)
L-09-BIOXHIT	A short report on the PSI contribution to WP 2.1 and WP 3.5	Clemens Schulze-Briese, Partner 4 (clemens.schulze@psi.ch)
L-10-BIOXHIT	Section 3 Overview	Colin Nave, Partner 3 (c.nave@dl.ac.uk)
L-11-BIOXHIT	Kappa Goniometry	Sandor Brockhauser, Partner 1B (brockhauser@embl-grenoble.fr)
L-12-BIOXHIT	Radiation damage detection, mitigation and exploitation	John McGeehan, Partner 1B (mcgeehan@embl-grenoble.fr)
L-13-BIOXHIT	BIOXHIT training activities – Section 6 overview	Sine Larsen, Partner 16 (sine@ccs.ki.ku.dk)
L-14-BIOXHIT	Presentation of TID centre Oulu	Rik Wierenga, TID Centre Oulu (rik@sun3.oulu.fi)
L-15-BIOXHIT	The BIOXHIT TID Centre in Poznan	Wojtek Rypniewski, TID Centre Poznan (wojtekr@ibch.poznan.pl)
L-16-BIOXHIT	Section 4 overview	Gerard Bricogne, Partner 5 (gb10@globalphasing.com)
L-17-BIOXHIT	Molecular Replacement	Garib Murshudov, Partner 8 (garib@ysbl.york.ac.uk)
L-18-BIOXHIT	Data modelling techniques	Peter Keller, Partner 5 (pkeller@globalphasing.com)
L-19-BIOXHIT	EMBLEM Technology Transfer	Thorsten Schneider, Partner 20 (schneider@embl-em.de).

Table 3c. BIOXHIT posters presented at the 3rd annual Project meeting in Didcot (February 2007).

Poster no.	Poster title	Scientist and Partner number of main author (email address)
P-01	The BIOXHIT Project	Victor Lamzin, Partner 1A (victor@embl-hamburg.de)
P-02	CCP4i Data tracking in the structure determination software pipeline	Peter Briggs, Partner 10 (p.j.briggs@dl.ac.uk)
P-03	A potential macromolecular test crystal system for the assurance of beamline quality	Annette Faust, Partner 1A (faust.annette@embl-hamburg.de)
P-04	Metal content analysis of protein samples with TXRF	Gerd Wellenreuther, Partner 1A (gerd.wellenreuther@embl-hamburg.de)
P-05	Improvement of Atomic Positions in Peptides	Helene Doerksen, Partner 1A (helne.doerksen@embl-hamburg.de)
P-06	Auto-Rickshaw: An automated Crystal Structure Determination Platform as efficient tool for validation of an X-ray diffraction experiment	Santosh Panjekar, Partner 1A (Panjekar@embl-hamburg.de)
P-07	Determination of protein secondary structural content from raw X-ray diffraction data: application for molecular replacement	Andrey Bogomolov, Partner 1A (Andrey.bogomolov@embl-hamburg.de)
P-08	The Use of Longer X-ray Wavelengths in Macromolecular Crystallography	Manfred Weiss, Partner 1A (msweiss@embl-hamburg.de)
P-09	Advancement of the software BEST for optimal planning of X-ray data collection from protein crystals	Alexander Popov, Partner 1A (sasha@embl-hamburg.de)
P-10	Beam Diagnostics and Data Collection Control at MAX-lab	Thomas Ursby, Partner 15 (thomas.ursby@maxlab.lu.se)
P-11	Remote Webservices	Venkataraman Pathasarathy, Partner 1A (pvenka@embl-hamburg.de)
P-12	The BIOXHIT Homepage and Database	Andrea Cristofori, Partner 1A (candrea@embl-hamburg.de)
P-13	Status of the Control system of the EMBL BW7B Sample changer	Uwe Ristau, Partner 1A (ristau@embl-hamburg.de)
P-14	The High Throughput crystallization Facility at the Centre for Integrated Structural Biology	Jose Antonio Marquez, Partner 1B (marquez@embl-grenoble.fr)
P-15	Regulating the <i>Escherichia coli</i> ammonia channel: the crystal structure of the AmtB-GlnK complex	Fritz Winkler, guest
P-16	An X-Ray Fluorescence (XRF) Detector based on Si Drift Technology (SDD) Optimized for Protein Crystallography	Martin Fuchs, Partner 9 (fuchs@bessy.de)
P-17	Kinetic protein crystallography using two wavelengths reveals the 8-oxo-dGTP hydrolysis mechanism of MutT	Teruya Nakamura, guest

P-18	Protein Information Management System (PIMS)	Anne Pajon, Partner 1C (pajon@ebi.ac.uk)
P-19	Xtal RECOgnition - Advanced Sample Centring	Tilo Strutz, Partner 1A (strutz@embl-hamburg.de)
P-20	Increasing the Ease and Speed of Eukaryotic Protein Expression: A Cell-Free In Vitro Translation System Based on Sf Insect Cell Extracts	Paul Donaghy, guest
P-21	The Oeiras TID Center	Daniele de Sanctis, TID Oeiras, (sanctis@itqb.unl.pt)
P-22	Automatic crystal centring and crystal optimisation on the SRS	Myrajan Muthusamy, Partner 3 (m.muthusamy@dl.ac.uk)
P-23	Conjugated Bile Acid Hydrolase Is a Tetrameric N-Terminal Thiol Hydrolase with Specific Recognition of Its Cholyl but Not of Its Tauryl Product	Maksim Rossocha, guest
P-24	autoPROC - a framework for automated data processing	Clemens Vornrhein, Partner 5, (vornrhein@globalphasing.com)
P-25	Novel cell-free expression system for synthesis of proteins used in structural analyses	Winfried Girg, guest
P-26	Automated centring of cryocooled samples with C3D	Bernard Lavault, Partner 1B (lavault@embl-grenoble.fr)
P-27	Greek TID Center for BIOXHIT	Renate Gessman, TID Heraklion (renate@imbb.forth.gr)
P-28	Transmissive X-ray beam position monitors (XBPM) based on fluorescent foils and on thinned position sensitive detectors (PSD), Task 2.1.2	Martin Fuchs, Partner 9 (fuchs@bessy.de)

The large number of participants and the fact that more registrations were received than could be accepted due to security limitations at the venue demonstrates that many BIOXHIT tasks are well advanced and ready for a wider dissemination to the scientific community. It also portrays the close cooperation of BIOXHIT with related EU-projects. Finally, it shows that BIOXHIT is a project with high visibility and a strong impact in the scientific community.

During the third year of the project, several workshops or ad-hoc meetings on specific scientific topics have been organised, Table 4. They covered not only activities from all scientific sections as well as the training activities organised by the BIOXHIT TID centres, but were also often collaborations with other projects, such as PIMS or DNA. 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 a close and productive cooperation 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 third year.

No.	Workshop title	Date and location
1	Working group 1 BIOXHIT/PIMS meeting on crystallisation	13-17 February 2006, Grenoble, France
2	Working group 2 meeting on data modelling for “smart data collection”	22-24 February 2006, ESRF Grenoble, France
3	MAXINF2 Integration workshop, Hamburg, Germany	27 February 2006, EMBL Hamburg, Germany
4	1st Oulu BIOXHTI workshop on protein crystallography, Oulu, Finland	2-4 May 2006, TID centre Oulu, Finland
5	8th International School on the Crystallography of Biological Macromolecules ^{a)}	21-25 May 2006, Società del Casino, Teatro Sociale, Como, Italy
6	Kappa working group meeting	6 June 2006, SOLEIL, France
7	DNA meeting at DIAMOND, Didcot, UK	29-30 June 2006, Didcot, UK
8	BESSY-PX satellite workshop at Bessy	5 September 2006, Bessy, Berlin, Germany
9	SHELX MAXINF workshop on Experimental Phasing of Macromolecules	5-7 September 2006, Bessy, Berlin, Germany
10	Meeting of the BIOXHIT TID Centres	7-8 September 2006, ESRF, Grenoble, France
11	BIOXHIT cross-section developers meeting on data tracking	14-15 September 2006, Daresbury, UK
12	BioCrys course on Fundamentals of Modern Methods in Biocrystallography	6-13 October 2006, TID Centre Oeiras, Portugal
13	Working group 1 BIOXHIT/PIMS meeting on crystallisation	18-19 October 2006, Amsterdam, The Netherlands
14	Workshop on the application of DNA/ BEST/ MOSFLM/ SCALA	18-19 October 2006, TID Centre Oulu, Finland
15	3rd TID workshop on Structural Biology with Synchrotron Radiation	28 November – 2 December 2006, TID Centre Poznan, Poland

^{a)} organised by A. Perrakis (Partner 6), A. Carfi and S. Di Marco under the auspices of the EU Network MAX-INF2 with a financial contribution from BIOXHIT.

Dissemination of both, the objectives and the results of BIOXHIT has again been an important activity in the third project year. 105 lectures have been presented by BIOXHIT Partners on various occasions. 56 posters have been displayed at conferences, and 21 articles referring to the project tasks (include those in scientific peer-reviewed journals) have been published. Further dissemination activities include the regular updates of the official project web site www.bioxhit.org, and a BIOXHIT slide show, which is also published on the project web site. The information on the project is widely disseminated via the Internet and the number of web links mentioning the project has, on average, increased from about 600 to 900 over the third year, Table 5.

Table 5. Number of Google hits for the search of ‘BIOXHIT’ during 2006

Date	Entries	Monthly average
03-Jan-06	566	607
10-Jan-06	641	
23-Jan-06	568	
31-Jan-06	651	
07-Feb-06	589	627
14-Feb-06	563	
21-Feb-06	747	
28-Feb-06	610	
07-Mar-06	582	650
14-Mar-06	595	
21-Mar-06	626	
28-Mar-06	797	
04-Apr-06	856	856
02-May-06	874	635
10-May-06	823	
16-May-06	738	
23-May-06	739	
30-May-06	734	
06-Jun-06	732	734
13-Jun-06	733	
20-Jun-06	713	
27-Jun-06	757	
04-Jul-06	840	858
11-Jul-06	805	
18-Jul-06	879	
25-Jul-06	907	
01-Aug-06	899	732
08-Aug-06	884	
15-Aug-06	897	
23-Aug-06	911	
29-Aug-06	967	
05-Sep-06	845	820
12-Sep-06	813	
19-Sep-06	814	
26-Sep-06	808	
13-Oct-06	802	803
17-Oct-06	814	
24-Oct-06	813	
31-Oct-06	781	
07-Nov-06	820	855
14-Nov-06	834	
21-Nov-06	870	
28-Nov-06	894	
05-Dec-06	881	883
12-Dec-06	861	
19-Dec-06	906	

In addition to the two existing BIOXHIT Training, Implementation and Dissemination (TID) centres in Oulu, Finland, (<http://www.biochem oulu.fi/BIOXHITWEB/index.html>), and in Poznan, Poland (<http://tid.ibch.poznan.pl/>), two further TID centres were established in 2006: one is located at the IMBB-FORTH in Heraklion, Greece (<http://www.imbb.forth.gr/people/petratos/index.html>), and the other at ITQB-Instituto Tecnologia Quimica e Biologica in Oeiras, Portugal (<http://tid.itqb.unl.pt/>). As with the first centres, the two new centres are building up their facilities using the seed funds provided by BIOXHIT. They are capable of disseminating BIOXHIT results to the wider scientific community in their own countries and the Portuguese TID Centre has already held a course on fundamentals of modern methods in biocrystallography. The TID centre in Poznan successfully held 2 workshops on “Biocrystallography using synchrotron radiation” in 2005, which attracted participants from several European countries and held one at end of 2006 along the same lines. A further workshop is planned for 2007. The TID Centre in Oulu held its first workshop in summer 2006. Due to its success it was followed by another workshop along the same lines in October 2006.

Three Project Steering Committee (PSC) meetings were held in January, May and a two-day meeting in October 2006. The next PSC meeting is scheduled for February 2007 in conjunction with the 3rd BIOXHIT Annual Meeting.