Executive Summary of 1st BIOXHIT Annual Report

The BIOXHIT project was launched on January 1st, 2004 with the aim of providing a new generation of effective tools for understanding complex biological processes at the molecular level. Within its projected lifetime of four years and with about 10 MEUR of EC funding, the BIOXHIT Partners will develop, assemble and deliver an integrated platform for high-throughput structure determination using X-ray crystallography with synchrotron radiation. X-ray crystallography is the method of choice for expanding the scope of structural studies in biology to the scale of entire genomes by virtue of its accuracy, of its speed, and of its potential for further speed gains; while synchrotron radiation is indispensable because of its spectacular intensity, coherence and tuneability properties. BIOXHIT is coordinating scientists at all European synchrotrons and leading software developers in both academic and industrial groups in a timely and unprecedented joint effort. The complexity of the project and the inter-dependence of its research tasks have been addressed by putting in place an efficient three-tier management structure. An essential part of the project is a proactive training effort for further dissemination at both synchrotron facilities and at satellite centres. The developments in BIOXHIT will be of lasting benefit to European research, underpinning European efforts in Structural and Functional Genomics, and thus playing an essential role in enabling Europe to maintain a leading position in this field at a time of intense effort and vigorous developments in the US and Japan.

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 and its interfaces with the logistics of protein production and crystallisation. Once deployed and tested, it will be made fully accessible to the wider life sciences research community through remote access facilities and an extensive program of training and dissemination. BIOXHIT objectives involve coordinated activities in hardware and software developments, the design of innovative experimental protocols, the establishment of European standards, and in high-level training. Within its lifetime of four years, the BIOXHIT project will have a major impact in the areas of protein crystallisation, of synchrotron beamline technologies, of sample handling and characterisation, of protocols for diffraction experiments and structure determination, and especially on the design and implementation of software architectures capable of supporting the progressive integration of all these steps.

The BIOXHIT project started officially on January 1st, 2004 (the complete list of Partners comprising scientists at all European synchrotrons and leading software developers in both academic and industrial groups is given in Table 1). However, its real launch followed the project kick-off meeting that was held in Hamburg in April 2004 with a total of 87 participants. Within the first year of the project, 32 scientists have been appointed at the various Partners' institutions to work on BIOXHIT goals. Despite the delay in hiring, which resulted in some of the project tasks starting later than planned, the overall activities of the project are well underway. The first BIOXHIT Annual Meeting, attended by 65 BIOXHIT participants, was held in Barcelona on December 1-4, 2004 as part of an EU Joint Meeting for projects in Structural Genomics and Proteomics. Significant advances were reported in many activity areas of the project, and the first-year achievements summarised in Tables 2, 3 and 4 were enthusiastically received by the members of the BIOXHIT consortium, the project Scientific Advisory Board, the Commission, and the other participants at the Barcelona conference.

Table 1. BIOXHIT Partners and their institutions.

Partner Role*	Partner Number in Annex 1	Partner Number 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

* CO = Coordinator, CR = Contractor, TP = Third Party

Table 2. Overview of the status of the BIOXHIT activities given in the 1-18 months implementation plan.

Section	Work packages	Tasks	Milestones (months 1-18)	Milestones achieved by month 12	Deliverables (months 1-18)	Deliverables scheduled by month 12	Deliverables achieved by month 12
1-7	26	87	50	18	68	17	18

BIOXHIT is well on schedule, despite the delay in hiring. From the data presented in Table 2, it can safely be expected that the 18-month milestones and deliverables will be met in time. Indeed, of the 17 deliverables scheduled by month 12, 15 have been achieved. This is undoubtedly a consequence of the efficient monitoring of Partners' activities built into the management structure of BIOXHIT. However it also reflects the fact that many Partners mobilised resources, which were not funded from BIOXHIT.

Table 3. Scientific BIOXHIT highlights, presented as posters during the first annual project meeting in Barcelona (December 2004).

Poster no.	Poster title	Scientist and Partner number coordinating the poster (email address)
1	Section 1: HTP protein crystallisation in BIOXHIT: achievements and perspectives	Christian Cambillau, Partner 11 (cambillau@afmb.cnrs-mrs.fr)
2	Section 1: Automated evaluation of crystallisation experiments	Julie Wilson, Partner 8 (julie@ysbl.york.ac.uk)
3	Section 2: X-ray beam position monitors	Martin Fuchs, Partner 9 (fuchs@bessy.de)
4	Section 2: Test crystal system	George Sheldrick, Partner 12 (gsheldr@shelx.uni-ac.gwdg.de)
5	Section 3: Crystal detection in loops	Babu Pothineni, Partner 1A (babu@embl-hamburg.de)
6	Section 3: The DNA initiative	Colin Nave, Partner 3 (c.nave@dl.ac.uk)
7	Section 4: Automated structure determination pipeline	Santosh Panjikar, Partner 1A (panjikar@embl-hamburg.de)
8	Section 4: Reorienting crystals	Sandor Brockhauser, Partner 1B (sudol@embl-grenoble.fr)
9	Section 5: BIOXHIT data management for PX structure determination	Peter Briggs, Partner 10 (p.j.briggs@dl.ac.uk)
10	Section 5: BIOXHIT Guidelines for data exchange	Avi Naim, Partner 1C (naima@ebi.ac.uk)
11	Section 6: BIOXHIT training activities	Sine Larsen, Partner 16 (sine@ccs.ki.ku.dk)
12	Section 7: General project poster	Victor Lamzin, Partner 1A (victor@embl-hamburg.de)

Highlights of the scientific goals already achieved were presented at the Barcelona meeting, not only within the BIOXHIT-specific sessions, but also as posters visible to the general audience. The complete list of BIOXHIT posters is given in Table 3. This demonstrates that some of the BIOXHIT tasks are already well advanced and are almost ready for a wider dissemination to the scientific public.

A notable feature of the overall pattern of activities presented in these posters is the considerable and unprecedented degree of collaboration they have entailed between groups of scientists associated with various European synchrotrons, who had previously followed their own lines of development in seeking solutions to problems of logistics and automation. The fundamental prerequisite to the success of BIOXHIT – namely 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 therefore been emphatically fulfilled.

Dissemination of both the objectives and the results of BIOXHIT has been an important activity in this first year. Over 80 lectures have been presented by BIOXHIT Partners on various occasions. 15 BIOXHIT posters have been presented at conferences, and 19 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.

Table 4. BIOXHIT workshops held during the first year.

Workshop no.	Workshop title	Date, location and attendees
1	**Section 2:** Automated X-ray provision	ESRF, Grenoble, France, 3rd- 4th May 2004, 55 attendees
2	**Section 5:** data and sample pipelining (a joint BIOXHIT-eHTPX-DNA workshop)	EBI, Hinxton, UK, 2nd July 2004, 40 attendees
3	**Section 2:** Synchrotron sources	EMBL, Hamburg, Germany 15th-18th September 2004, 60 attendees from BIOXHIT and 140 other conference participants
4	**Sections 1 and 3:** Crystal recognition in drops and cryo-loops	Daresbury Laboratory, UK, 23rd-24th September 2004, 20 attendees
5	**Section 3:** Kappa workgroup meeting	EMBL Grenoble, France, 29th September 2004, 14 attendees

Five BIOXHIT workshops on specific scientific topics have been organised, Table 4. They represented activities on recognition and handling of macromolecular crystalline samples, automated systems for the provision and monitoring of X-ray beam, goniometric systems for X-ray data collection and software engineering aspects of data and sample pipelining. The latter workshop was held jointly with two UK-funded projects (eHTPX and DNA), which are related to a number of BIOXHIT tasks. In addition, within the EMBL Hamburg 30-years anniversary conference, a microsymposium on new synchrotron sources was organised. All of the workshops were well attended and provided a forum for fruitful interactions.

Further dissemination activities include the establishment of the official project web site www.bioxhit.org (launched in January 2004, redesigned in December 2004) and the design and the production of a project brochure.

Two BIOXHIT Training, Implementation and Dissemination (TID) centres have been established: one in Oulu (Finland) and one in Poznan (Poland). During the next project period, these two centres will have to build up their facilities using the seed funds provided by BIOXHIT. The setup facilities should be capable of disseminating BIOXHIT results to the wider scientific community in their own countries.

In order to complete the Management Team at EMBL Hamburg, Mrs. Daniela Jänicke has been appointed and made responsible for the administrative aspects of the project. Three Project Steering Committee (PSC) meetings were held in 2004 - one meeting in January, one in April in conjunction with the project kick-off meeting and one in December in conjunction with the first Annual Meeting in Barcelona.