Updated Science Cases – BioMAX

Facts

Title	BioMAX
External collaborations	Karolinska Institutet, Aarhus University, ESRF, Soleil, MXCuBE consortium, EMBL-Hamburg and more.
Original budget and funders	82.2 MSEK (KAW and 12 Swedish universities)
Official start	2011
Expected date of completion	End 2016, user program start early 2017, enhancements 2018 onwards

Introduction to the project

BioMAX is the first MX beamline at MAX IV providing the Nordic/Baltic structural biology community with an essential instrument for x-ray diffraction data collection. This is an important asset as more than 90% of all data leading to protein structures deposited in the protein databank are collected at synchrotrons and hence access to technical advanced beamlines is essential. The beamline has been constructed such that the experiment setup will be highly automated, in terms of both hardware and software. BioMAX aims to be robust and simple to operate with a beam benefiting from the properties of the MAX IV 3 GeV ring. Due to its extensive energy range, BioMAX is the ideal source for *de novo* phasing using anomalous dispersion. Thanks to its small beam size and very low divergence, BioMAX is an outstanding experimental setup for microcrystals and ultra large unit cells, which makes it an excellent beamline for data collections on membrane protein crystals as well as large complexes.

Development of new pipelines engaging the full capabilities of the hardware and software are important to guarantee efficient high-throughput data collection, which is important for fragment-ligand screening of proteins. Fragment-ligand screening of proteins by crystallography is becoming a major tool for drug-design purposes, but it can also provide more information on enzyme mechanisms and lead to new probes used in a cellular context in chemical biology experiments. For this purpose we are establishing the FragMAX fragment screening facility in close collaboration with the Lund University protein production platform LP3 and industrial collaboration partners like Astra Zeneca and SAROMICS.

Technical description of the project

BioMAX is based on an in-vacuum undulator, 18 mm period length, 4.2 mm minimal gap, 2 m magnetic length. The magnet structure is undulator the energy range between 5 and 25 keV. As optical elements, BioMAX has a Si (111) horizontally deflecting, LN2 side-cooled double crystal monochromator followed by a Kirkpatrick-Baez (KB) mirror pair with Si/Rh/Pt stripes for harmonic rejection. The experimental station is equipped with a high precision MD3 diffractometer, a high capacity automatic sample changer ISARA and the highest performance hybrid pixel detector currently available, the Eiger X 16M.

Design goals:

Energy range: 5-25 keV; energy resolution ΔE/E: $2x10^{-4}$; Flux at sample 2 x 10^{13} ph/s; Focus: 5 µm x 20 µm.

Experimental setup:

MD3: Sphere of confusion: 150 nm at 100 deg/sec; Sample centering mechanical resolution 200 nm; Beam shaping 5-50 µm diameter; Additional environments: mini-kappa goniometer, crystallization plate holder for *in-situ* measurements, Oxford Instruments Cryojet 5, HC-lab humidity control device, rapid cryo-HC-lab exchanger, Amptek fluorescence detector.

Eiger 16 M Detector: Number of pixels: 4150 × 4371 = 18'139'650; Pixel size; 75 × 75 μm^2; Sensitive area: 311.2 × 327.8 mm^2; Frame rate 16M/4M Mode 133 Hz/750 Hz.

ISARA sample changer: Number of samples: 100 in SPINE pucks, 304 in universal pucks; Plate screening 4 sbs-plates in plate loader; Sample exchange time: < 30 sec using universal pucks.

Development of automated data collection strategies using multi-crystal sample holders would be beneficial as sample exchange is becoming the rate limiting step in high-throughput approaches. Automated data processing and hit identification pipelines need to be refined. In addition, through collaboration with other partners MAX IV could provide fragment screens to academic users, thus promoting a wider use of these methods as while industry has been pioneering and implementing fragment screening, academia is lagging behind.

Present status of the project

The beamline optics have been installed and partially commissioned delivering a 20 x 5 μm^2 beam on the sample position. Further optimisation and commissioning of the optical elements including the undulator are on-going. In the experimental hutch the MD3 diffractometer and an Eiger 16M-detector have been installed. The general user program did start in March 2017. So far, a growing number of Swedish and international users from academia and industry have used BioMAX for their research.
For the user control software of the beamline we are one of the drivers in the development of MXCuBE v3 in main collaboration with the ESRF and other members of the MXCuBE consortium. We have implemented a new interface using modern html software technology leading.

Expected status summer 2019

In summer 2019, BioMAX will be in full user operation. Major capabilities from the design and choice of instrumentation should be available to the user community. Remote operation will be added and can be tested with friendly users. Energy tunability by the users will be achieved.

Major partners and additional funding

FRAGAMAX VR-funding, RÅC funding SSX project. We are members of the the MXCuBE and ISPyB-consortium. Adapting beam condition unit for precise low-resolution data collection for phasing purposes and membrane protein-lipid interactions EMBL-HH

Changes made since the start of the project

Only small adjustments have been made since the start of the BioMAX project in 2011.

Comparison to similar beamlines world wide

All major synchrotrons in the world provide beamlines for protein structure determination and as the community is large and is dependent on beamtime this is required.

The BioMAX beamline is a highly competitive beamline mainly through the combination of a relatively simple optical design and the superior MAX IV and it can compete with world-leading microfocus beamlines such in terms of flux and focus, while being stable and easy to use.

A limited number of beamlines dedicated to fragment screening have been developed. The major two beamlines currently are I04-1 at Diamond Light Source (UK) and BL14-2 at HZB-BESSY (Germany)

How do you see that the project could develop beyond 2023?

MX will remain a major technique for understanding protein structure and function and BioMAX will remain an essential instrument for the community. This requires that the beamline remains up-to-date and new technical advances such as the development of new detectors leading to more precise and faster data collection need to be implemented. As it is becoming apparent that structures collected at cryo-temperatures do not sample the full conformational landscape, or have altered ligand binding, room temperature data collection needs to be re-addressed as this would lead to more reliable information on the conformation and dynamics of proteins and their complexes. Radiation damage is a major problem for room data collection, therefore faster detectors for collecting more undamaged data per sample, new strategies using multi sample to serial crystallography approaches are tested and implemented.