

# Optimizing Sample Handling in Macromolecular Crystallography



## Grenoble, France

### The European Molecular Biology Laboratory (EMBL) utilizes HID Global RFID technology for automated handling of biological samples at cryogenic temperatures.

Located between the beautiful Alps of Grenoble, the European Synchrotron Radiation Facility (ESRF) produces X-ray beams that are 100 billion times brighter than the X-rays used in hospitals. This facility helps researchers from around the globe gain insight into the atomic and microscopic structure of matter. The macromolecular crystallography (MX) beamlines are particularly useful to study biological materials, develop highly efficient medicine and fight cancer more effectively.

*“The HID Global HF DBond™ technology has proven to be reliable against temperature cycling between room and liquid nitrogen temperatures, and the HID team in Switzerland was very supportive to help with our new designs.”*

Florent Cipriani,  
Head of Instrumentation Team,  
EMBL Grenoble

The European Molecular Biology Laboratory is a nonprofit organization, publicly funded by 26 member states, employing over 1.700 people on six sites in Europe. Located next to the ESRF, EMBL Grenoble is involved in the operation of MX beamlines, which are used to take pictures of biological macromolecules on an atomic level by hitting them with a thin intense x-ray beam after they have been prepared in a crystalized form and frozen. EMBL also designs and develops instruments used in this imaging method and selected RFID technology from HID Global in their latest developments.

### Challenges

Creating a high-resolution picture and subsequent 3D atomic model of a biological macromolecule is a complex process. After a macromolecule of interest (typically a protein) is isolated and purified, tiny crystals are grown, harvested, mounted and frozen on a sample holder in a loop set at the tip of a tiny needle. Once frozen, the crystals need to be stored in liquid nitrogen at -321°F (-196°C) and identified for further processing with the x-ray beam while remaining cool. It is often necessary to process a large number of crystals to obtain a high-resolution picture. Similarly, drug discovery requires testing large numbers of drug molecules to find those able to bind to the target protein, therefore processing large numbers of drug labeled protein crystals. This makes the automation of sample handling and sample tracking very important.

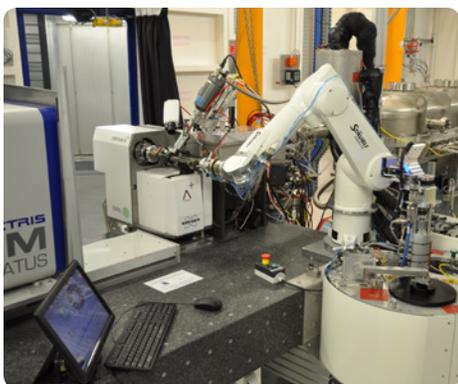
Most of the sample holders currently used in macromolecular crystallography offer limited storage density and poor initial crystal-positioning precision upon mounting on a goniometer. This has become a limiting factor at high-throughput beamlines, where data collection can be performed in a matter of seconds, especially as the number of crystals processed at ESRF rose above 200K/year.

Furthermore, the lack of precision of the sample holders limits the potential benefits of automated harvesting systems that could provide crystal-position information to quickly set the sample in the X-ray beams. This situation provided the motivation for the development of a compact and precise sample holder with corresponding storage pucks, handling tools and robotic transfer protocols. The sample identification methods must resist repeated cryogenic storage and be immune against readability issues due to frosting.

### EMBL MISSIONS

EMBL pursues five synergistic missions that, in combination, complement and provide added value to the activities of member state scientific communities.

1. Forefront research: uncovering the molecular basis of life
2. Providing world-class research infrastructure and services
3. Training and inspiring the next generation of leading scientists
4. Driving research, innovation and progress through technology development, interactions with industry and technology transfer
5. Playing a leading role in the integration of life science research in Europe



*“Using the miniSPINE system has been a great experience as it combines a high degree of user-friendliness with high-storage density. A very good way to facilitate sample handling at high throughput beamlines.”*

Dr. Jens Hausmann,  
EMBL Chemical Biology Core facility,  
Heidelberg



EMBL



European Molecular  
Biology Laboratory

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## Solution

Embeddable RFID tags from HID Global were chosen for sample identification, due to their tiny footprint and proven track record to work in cryogenic environments and the ability of HID for custom tag designs to meet the demands of EMBL. EMBL developed two new sample holder standards, “NewPin” and “miniSPINE”, which are optimized for high throughput frozen crystallography and include the embedded tags from HID Global.

### Design goals:

- Small footprint
  - for high storage density & reduced transport cost
- High precision
  - to facilitate crystal alignment at beamlines and
  - to benefit future automated crystal harvesting systems
- Reliable sample tracking
  - Puck tracking with RFID tags and DataMatrix
  - Optional pins tracking with RFID tags

RFID tag was embedded to reliably track the samples from the point they are harvested and stored frozen in cryo-containers to the point they are processed at beamlines utilizing robots for efficient and error-free sample handling.

## Results

The new RFID-enabled NewPin and miniSPINE sample holder standards for frozen Macromolecular X-ray crystallography share the same robot gripper. They also allow the storage of 36 to 64 sample holders in RFID identified pucks, which represents depending on the standard 252 to 448 samples in a dry-shipping Dewar commonly used in the field. The pucks are identified with human and machine readable codes, as well as with embeddable HF RFID tags from HID Global. The harvesting, cryogenic storage and beamline feeding process could be fully automated utilizing robot grippers and specifically designed RFID readers. This solves the readability issues due to frosting of traditional data matrix codes, increases throughput and prevents documentation errors. Available memory space in the RFID tags allows storing information like the puck manufacturer UID, the puck type and permits users to store and retrieve private samples information.

## Additional Benefits

Beyond the creation of these high performance sample holders and associated storage pucks, the cryo-resistant RFID technology adopted to identify the existing low-density sample storage pucks currently used in macromolecular crystallography.

Furthermore, this technology can also be used in cryo-electron microscopy, an alternative method to picture biological macromolecules at an atomic level. In this case, HID’s RFID technology will be used to identify and track the small boxes and pucks used to store sample grids in liquid nitrogen. This will be an important feature in service oriented cryo-electron microscopy platforms.