EMBL Grenoble

Structural biology

Future challenges - instrumentation-wise

EMBL Grenoble outstation

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www.embl.org

Two future challenges in Crystallography

1- Difficult projects
- Macromolecular assemblies
- Membrane proteins

MD3 sub micron precision diffractometer

μ crystals

***Large numbers** of Poorly diffracting crystals*

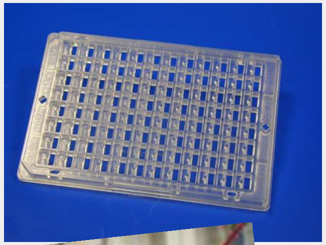
2- Benefit from future beamlines
- **EMBL@PETRA-III** High brilliance
  → ***A few 100 ms** crystal life time*

- **ESRF-UP beamlines**
  Ultra high brilliance
  Very low emittance
  → ***ms** crystal life time*
  → *All flux in a **1 μm²***

Samples delivery
*Process **μ crystals***

Screening

Crystal Direct



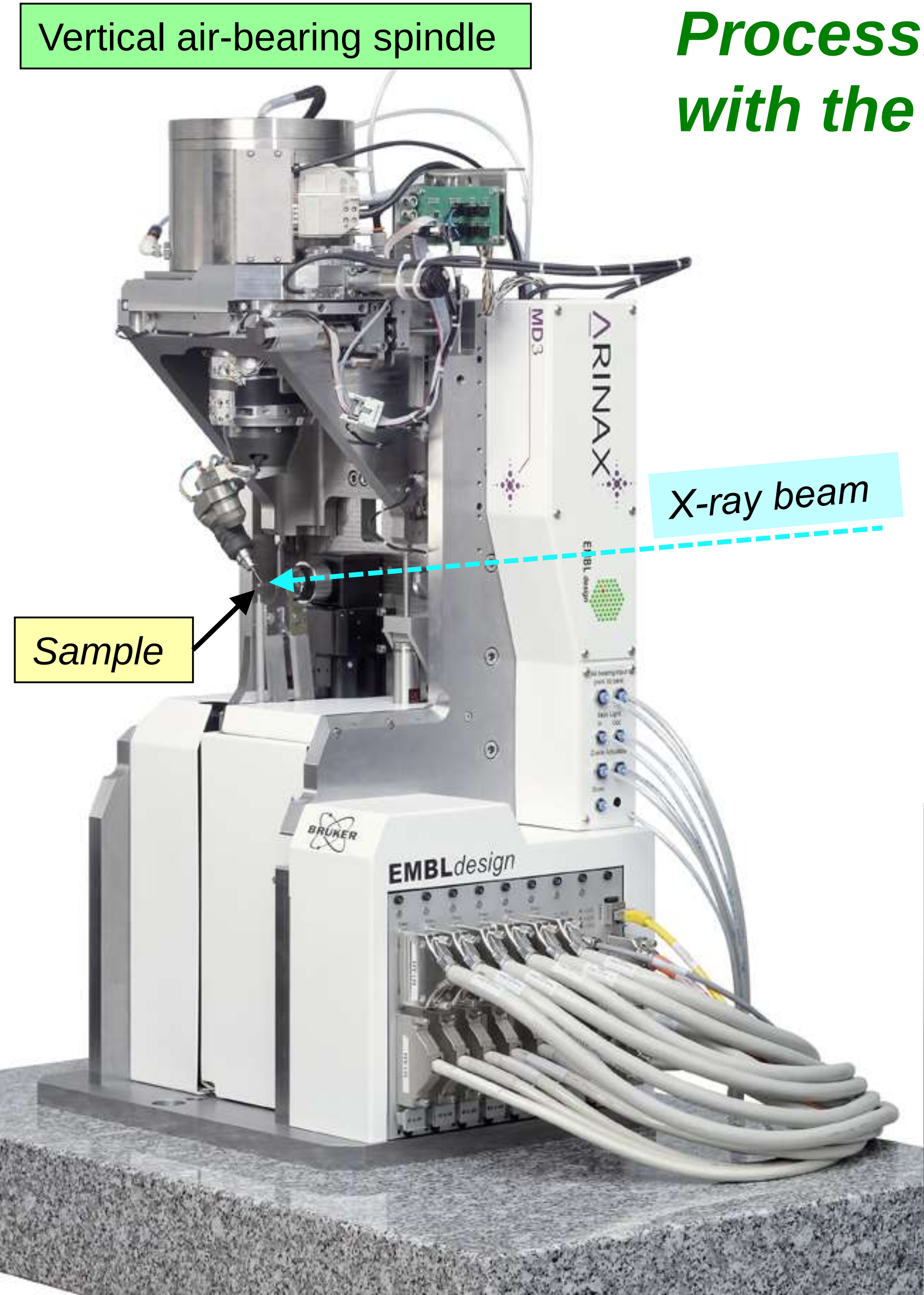
NewPin

Sample holder
for High density storage

In-Situ data collection

Automated harvesting

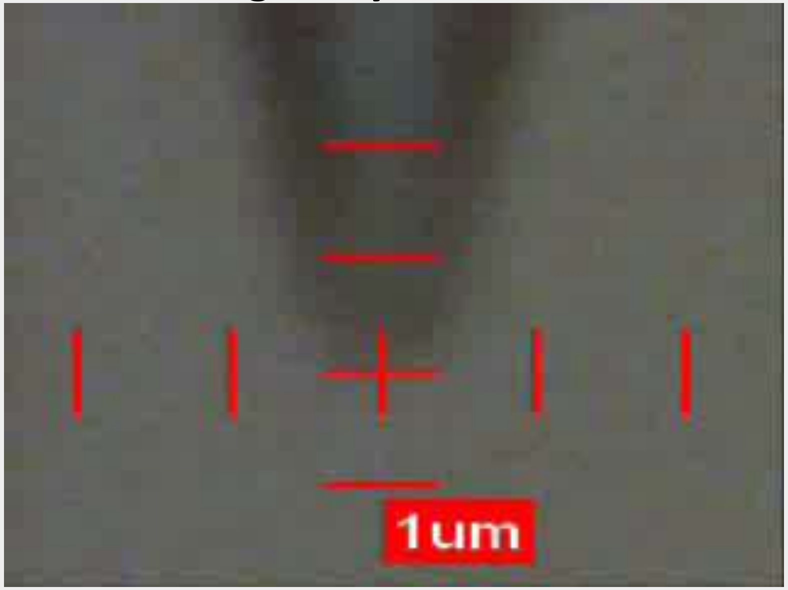
Processing micron sized crystals with the MD3 Kappa diffractometer



Motion error at sample position less than 50 nm

MD3 Vertical Kappa Diffractometer

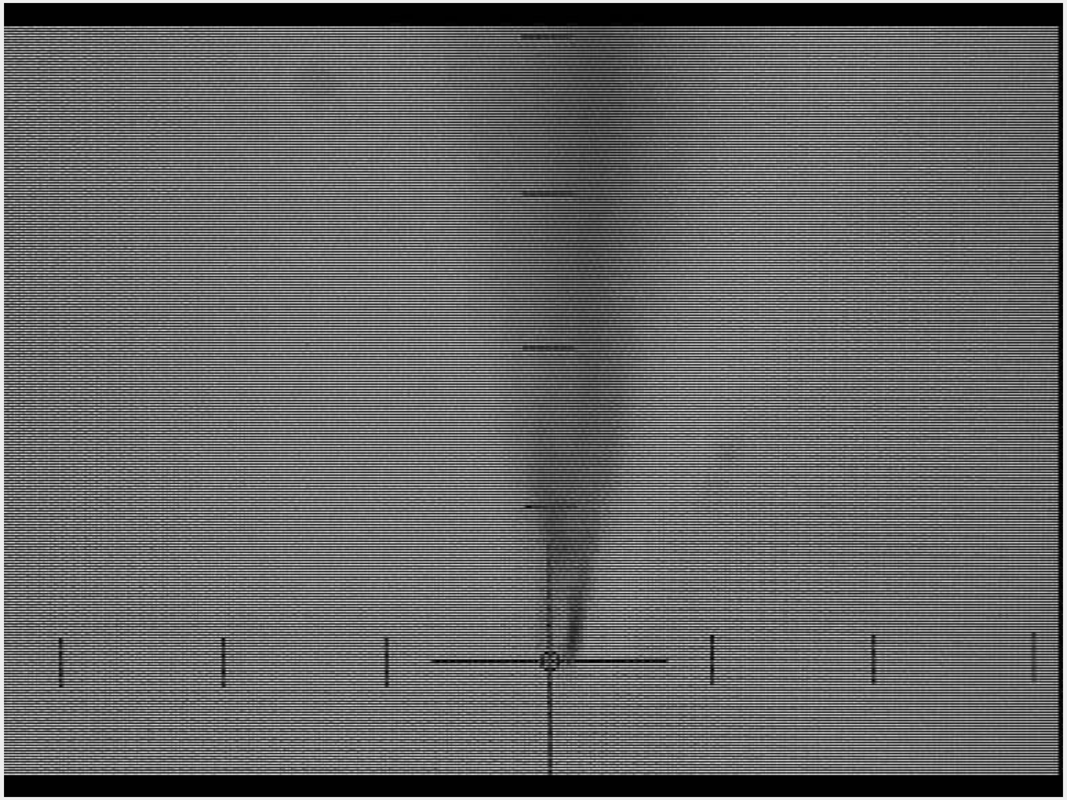
Omega only, Rotation 160° /s



Scale: 1 µm/div

Glass Needle 0.3 µm tip

Kappa = 48° , **Rotation** 20° /sec (Omega)



Scale: 10 µm/div

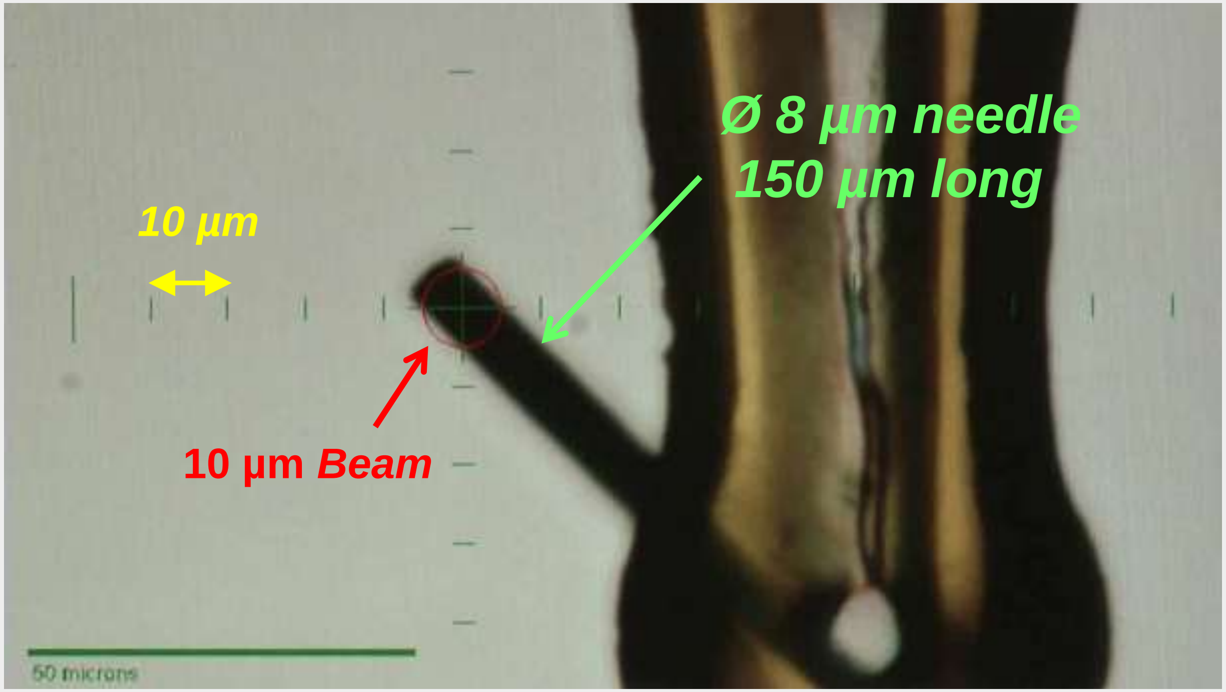
Circle: 1 µm diameter

Glass Needle 1 µm hole

MD3 High dynamic precision 4D Scan

Video: *4D Helical Scan* *along an* **8 µm needle**

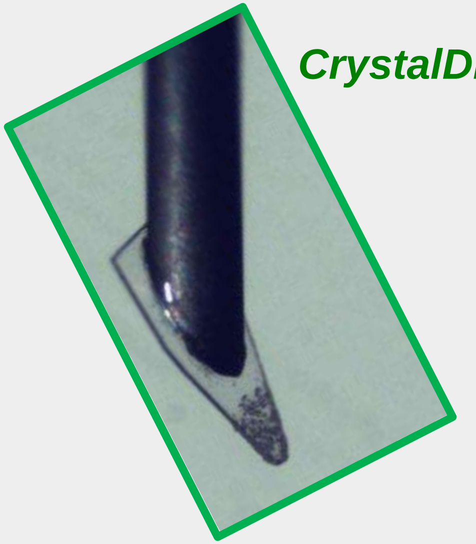
180 deg in 10 sec, Pilatus detector



Synchronous move of

- OMEGA (ang. scan)
- *Centring table (XY)*
- Alignment table (YZ)

SERIAL Data collection *over batches of micro-crystals*



▲ Fast data collection, over **full sample volume**

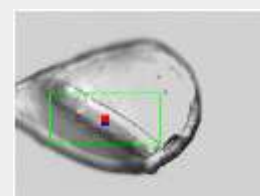
Towards full automation of crystallography…

Crystallization is automated

MX beamlines are automated

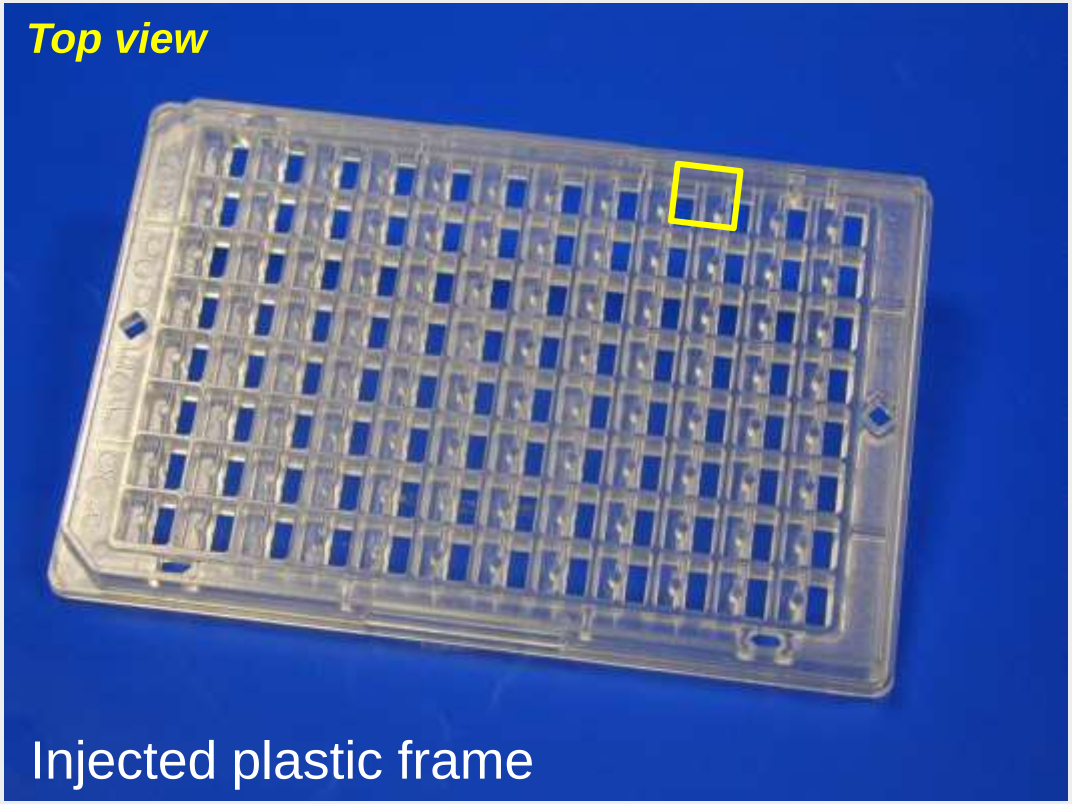
Today

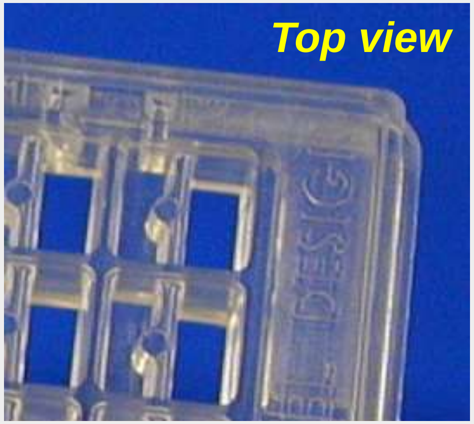
?

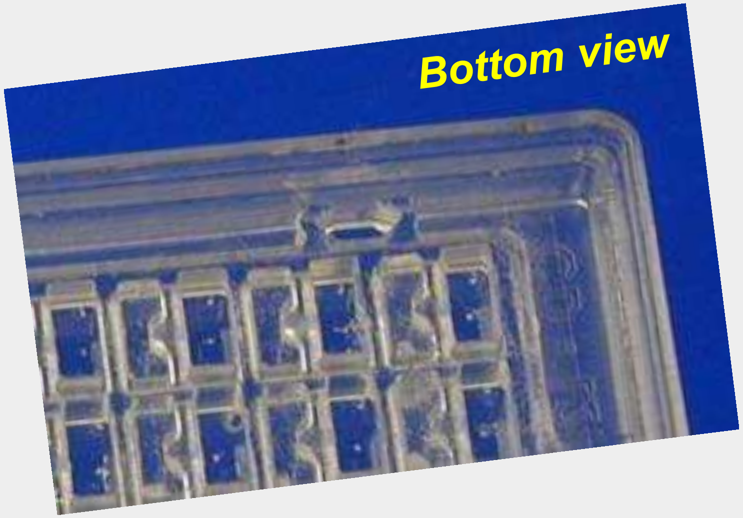


CrystalDirect™ concept: ***CD crystallization plates***

Crystals grow on an ultra thin films (Vapour diffusion)



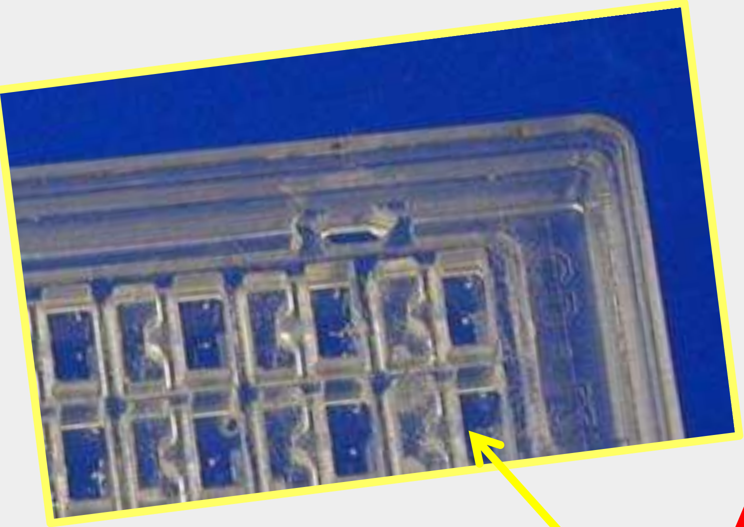


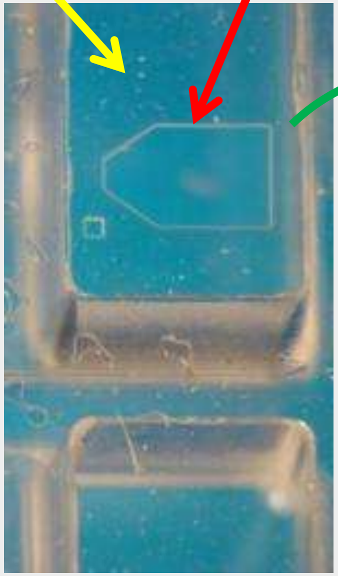


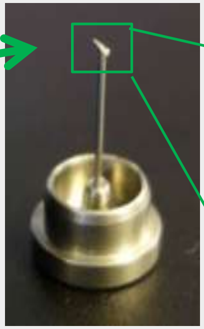
CrystalDirect™ concept: *Crystal Harvesting*

Cut with a fs laser beam

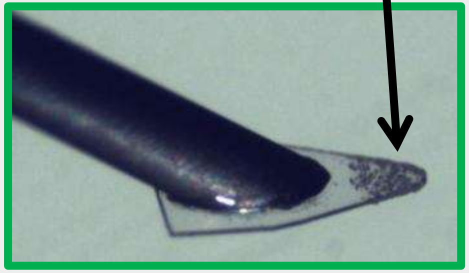
- **Photo ablation** → Cold plasma





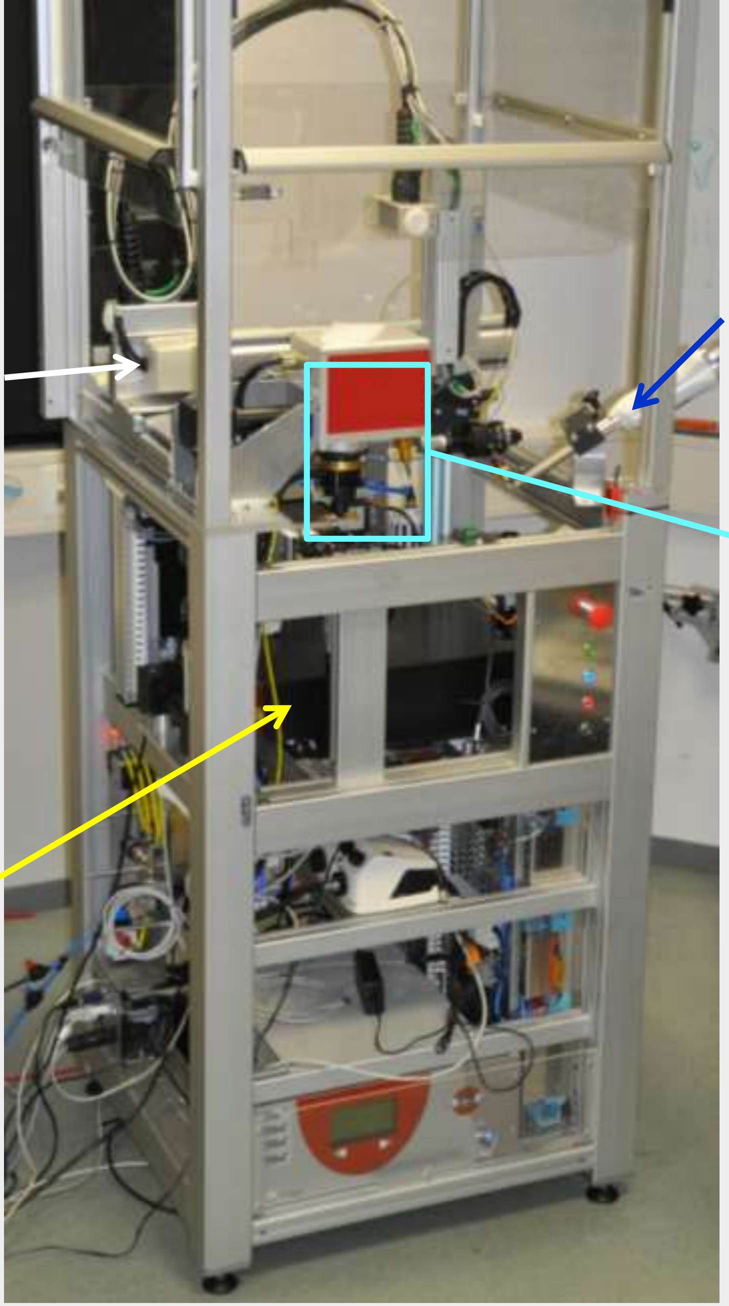


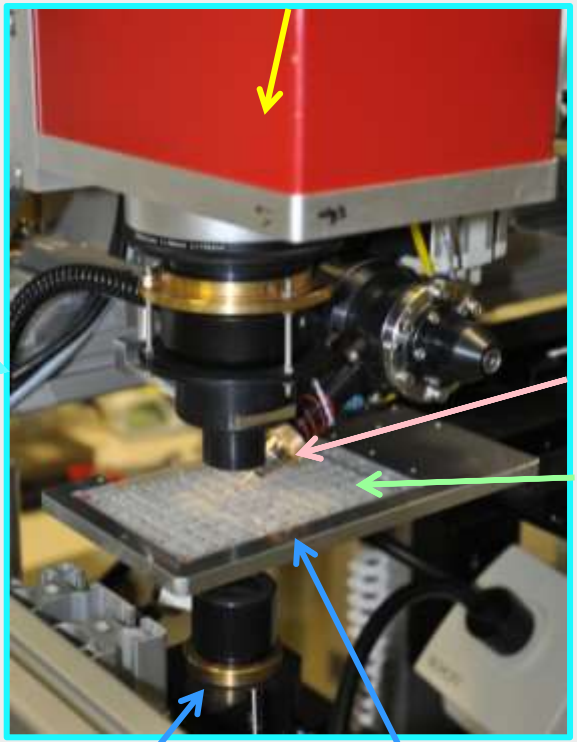
Crystal(s)



CD Harvester *prototype*

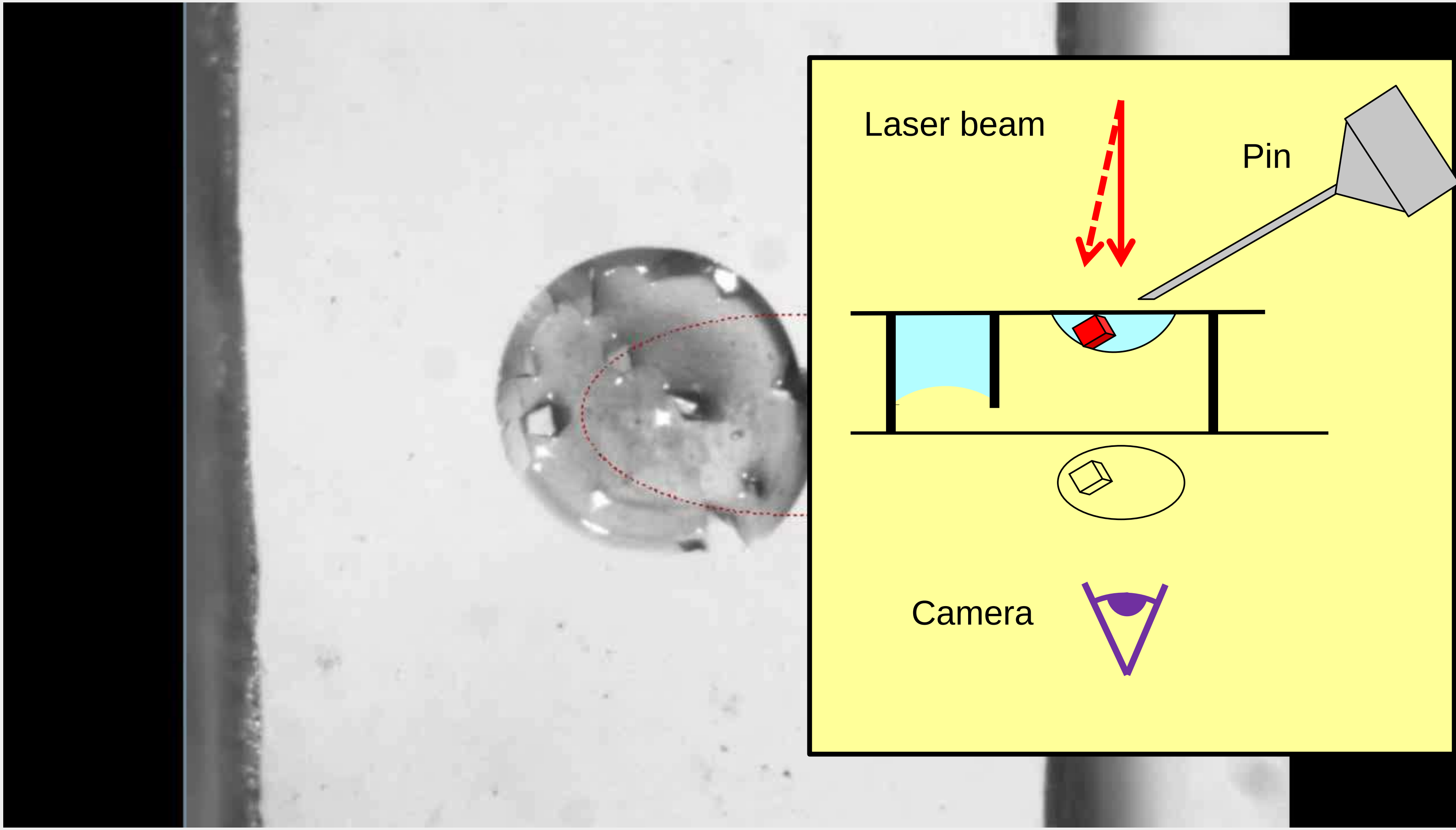
Harvest & Freeze one crystal





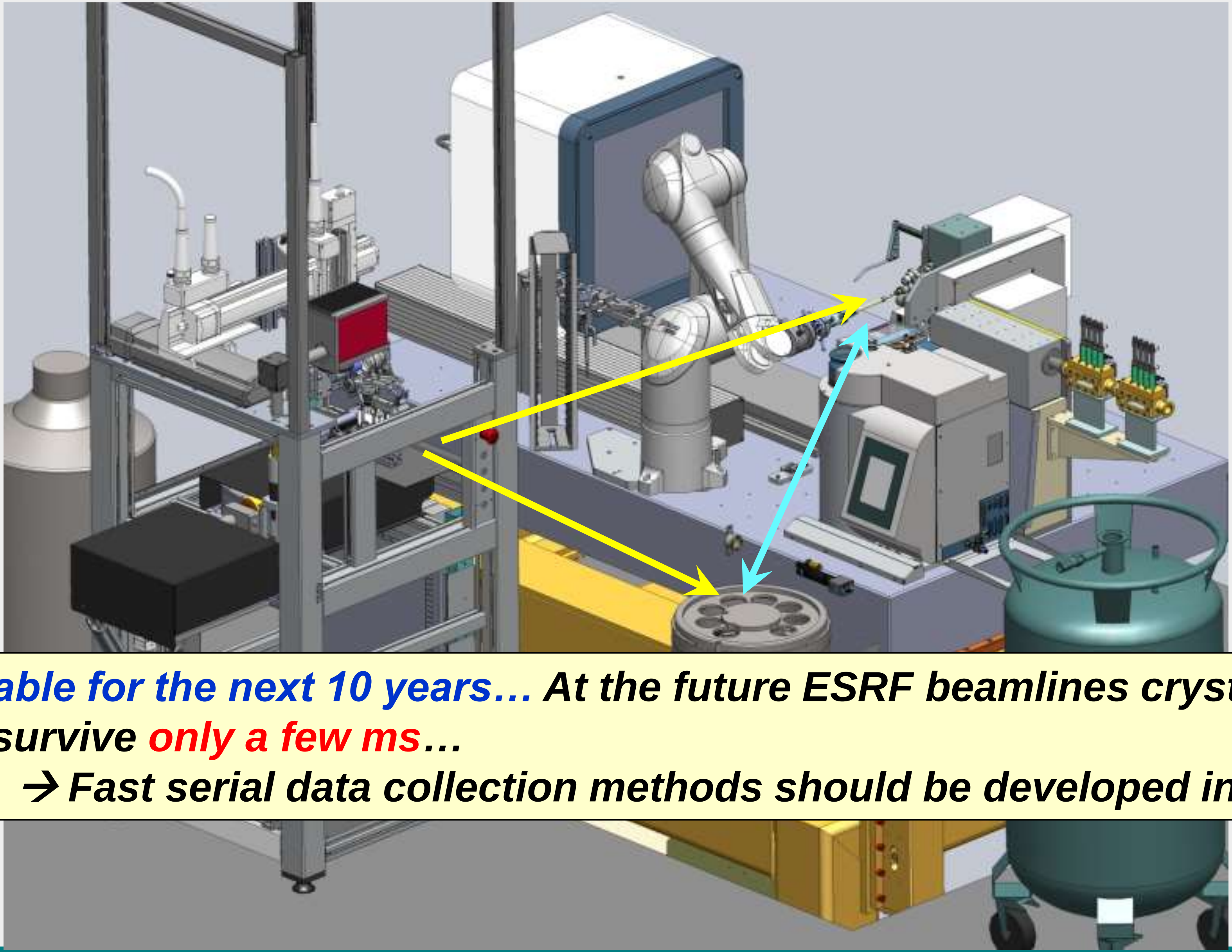
Connected to → *Cryo storage unit*
→ *Beamline SC*

CrystalDirect Harvesting process - video



(Bottom view)

Integration of a CD harvester on a beamline



Suitable for the next 10 years… At the future ESRF beamlines crystals will survive only a few ms…

→ Fast serial data collection methods should be developed in //

Conclusions

- Getting the best from the future beamlines will require re-thinking the sample environment

- Again automation will play a central role

- Solutions are already drawn, but critical point is funding
  Termination of current EU FP7 programs & the lack of visibility for the future…

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