An advanced example for 3D imaging of microscopic samples by proton tomography

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Interactions
Rayonnements
Ionisants et Biologie

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Outline

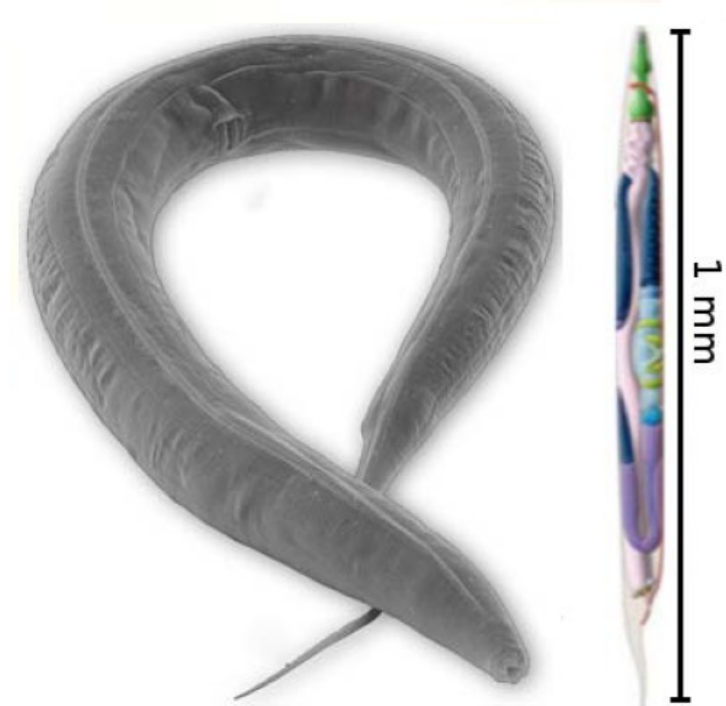
I. Context
   i. Proton imaging on *C.elegans*
      - STIM tomography
      - PIXE tomography
   ii. Reconstruction of tomographic images

II. Advanced example
   i. Construct phantoms
   ii. Define simulation parameters
   iii. Save the simulated data
   iv. Sort the data to model the detector

III. Results

IV. Perspectives

Proton imaging on *C. elegans*



iRiBio group – Ionizing Radiation interactions and Biology

Multidisciplinary research group:

Physics / Chemistry / Biology / Numerical modeling

Two themes are more specifically explored:

In-vitro and in-vivo nanotoxicology

Optimization of therapeutic approaches to proton therapy, and in particular combining irradiation by proton beam and metallic nanoparticles or metallic oxides

Methods:

Proton imaging on biological micro-organism like *Caenorhabditis elegans* (*C. elegans*), a small worm living in temperate soil environments

Proton imaging on *C. elegans*

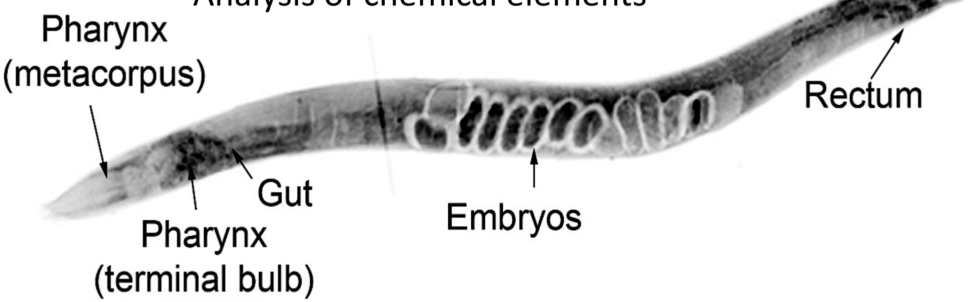
Objective:

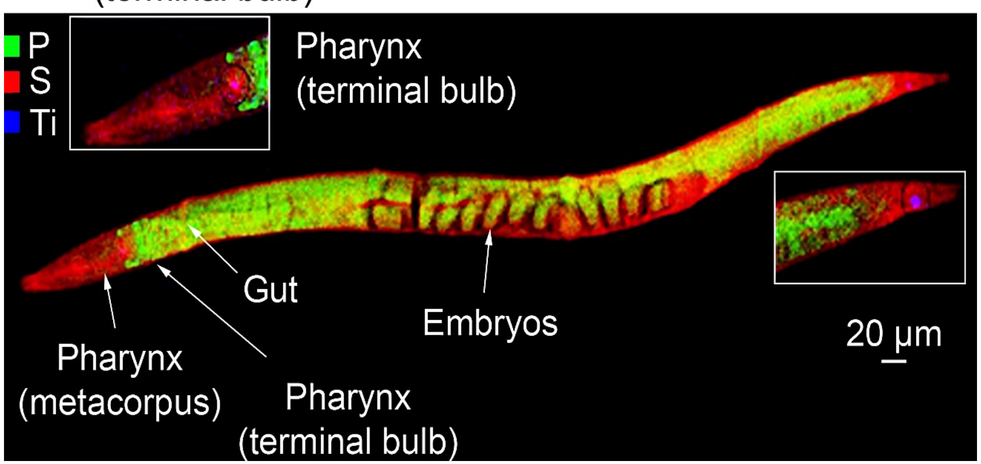
Understand the biological effects of contaminants, such as TiO2 nanoparticles, widely used in cosmetics, the food industry, paints, etc.

Methods:

STIM and PIXE tomography experiments

Analysis of chemical elements





Non-destructive techniques, do not require marking, coloring…

- Spatial resolution ~300 nanometers in vaccum
- Detection limit ~1 ppm

STIM: Scanning Transmission Ion Microscopy

Measurement of the residual energy of the protons after passing through the sample

→ Material thickness (g/cm^2)

→ Visualization of the internal structure

Density Contrast Imaging ≈ Proton "Radiography"

PIXE: Particle Induced X-ray Emission

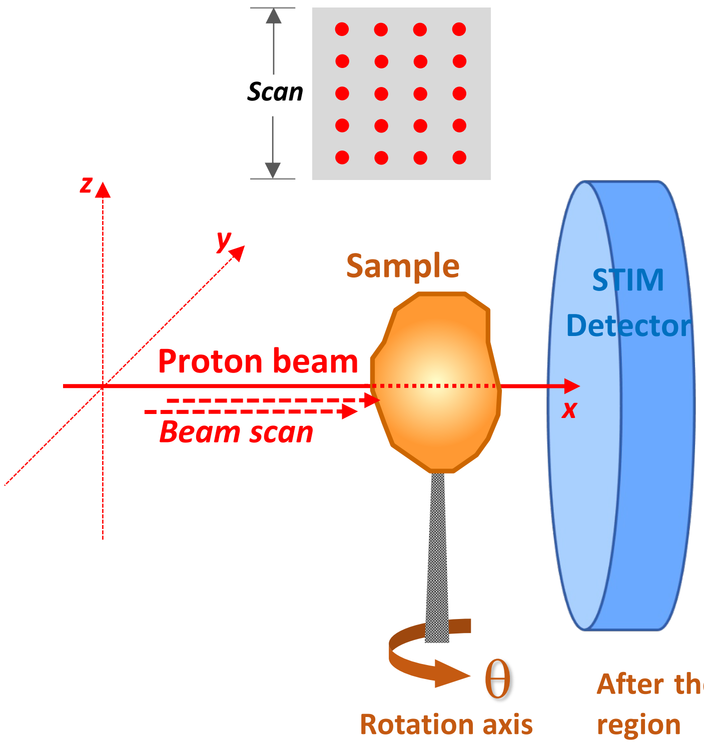
Measurement of the energy of emitted X-rays

→ Location of chemical elements

→ Quantification

Minerals, trace metals, exogenous elements (here the nanoparticles of TiO_2)…

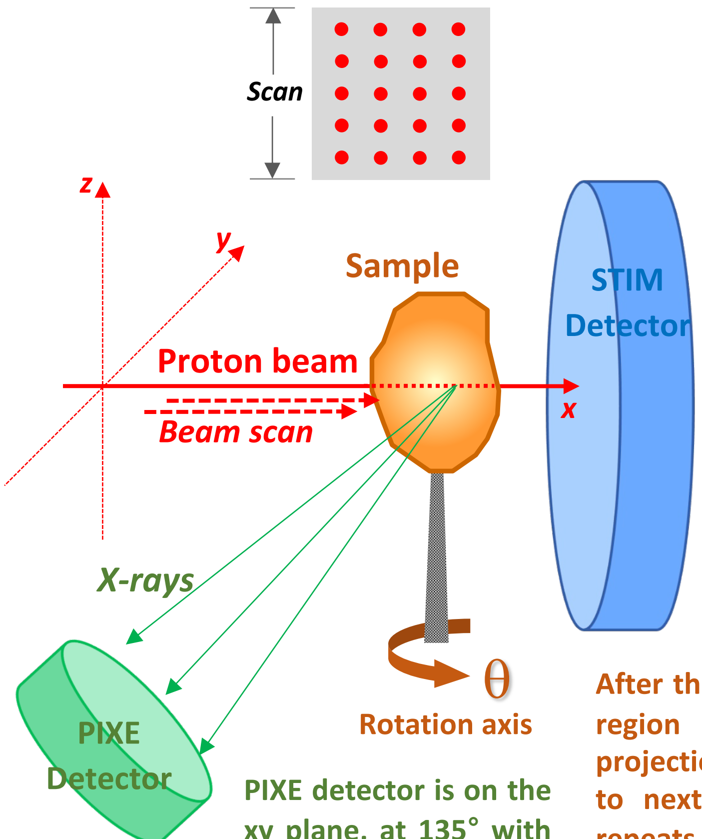
Experimental setup for STIM and PIXE tomography



STIM detetcor is placed after the sample.

After the beam finishes scanning the region of interest (ROI) for one projection angle, the sample rotates to next projection, and the beam repeats the scanning.

Experimental setup for STIM and PIXE tomography

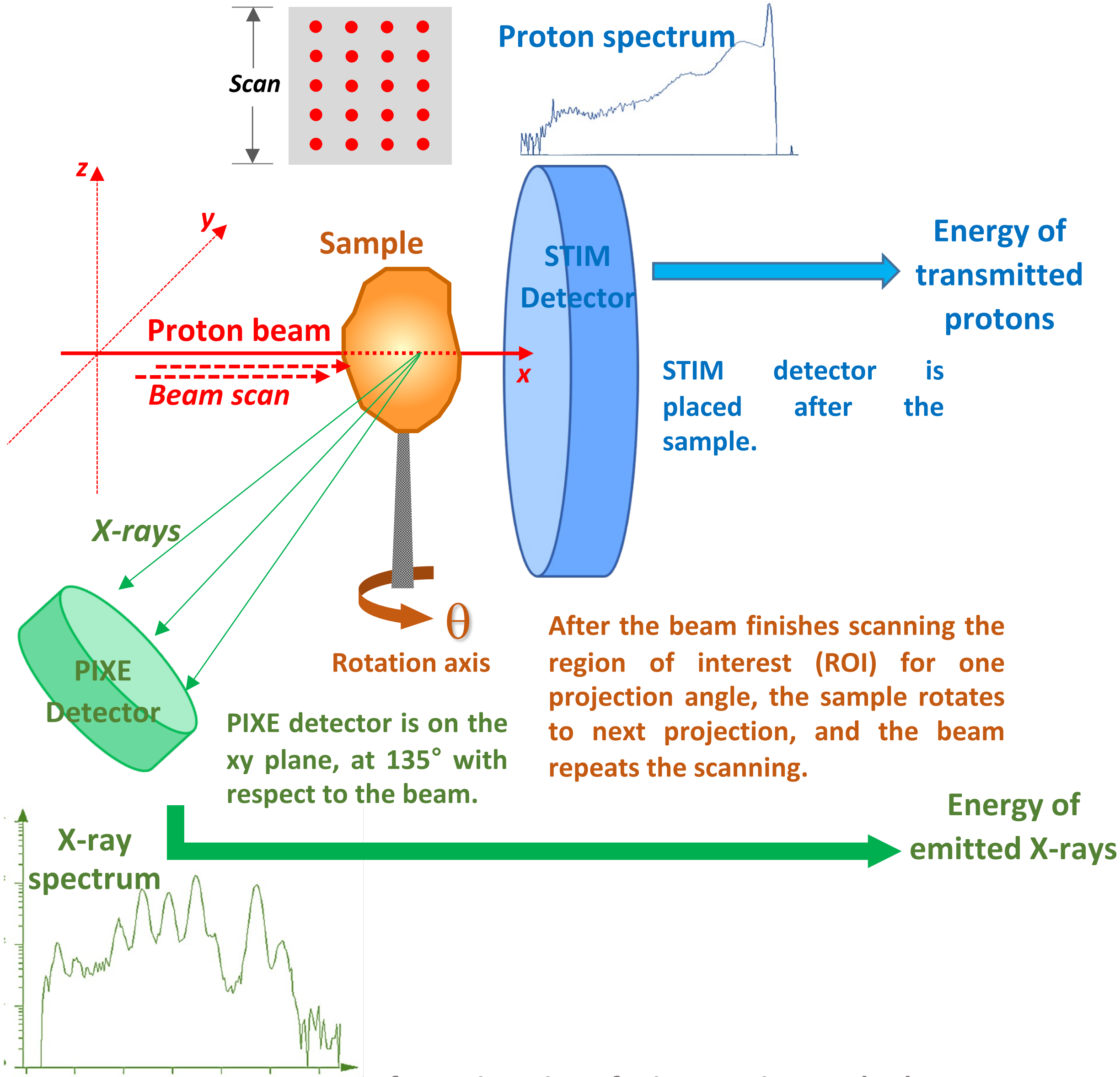


STIM detector is placed after the sample.

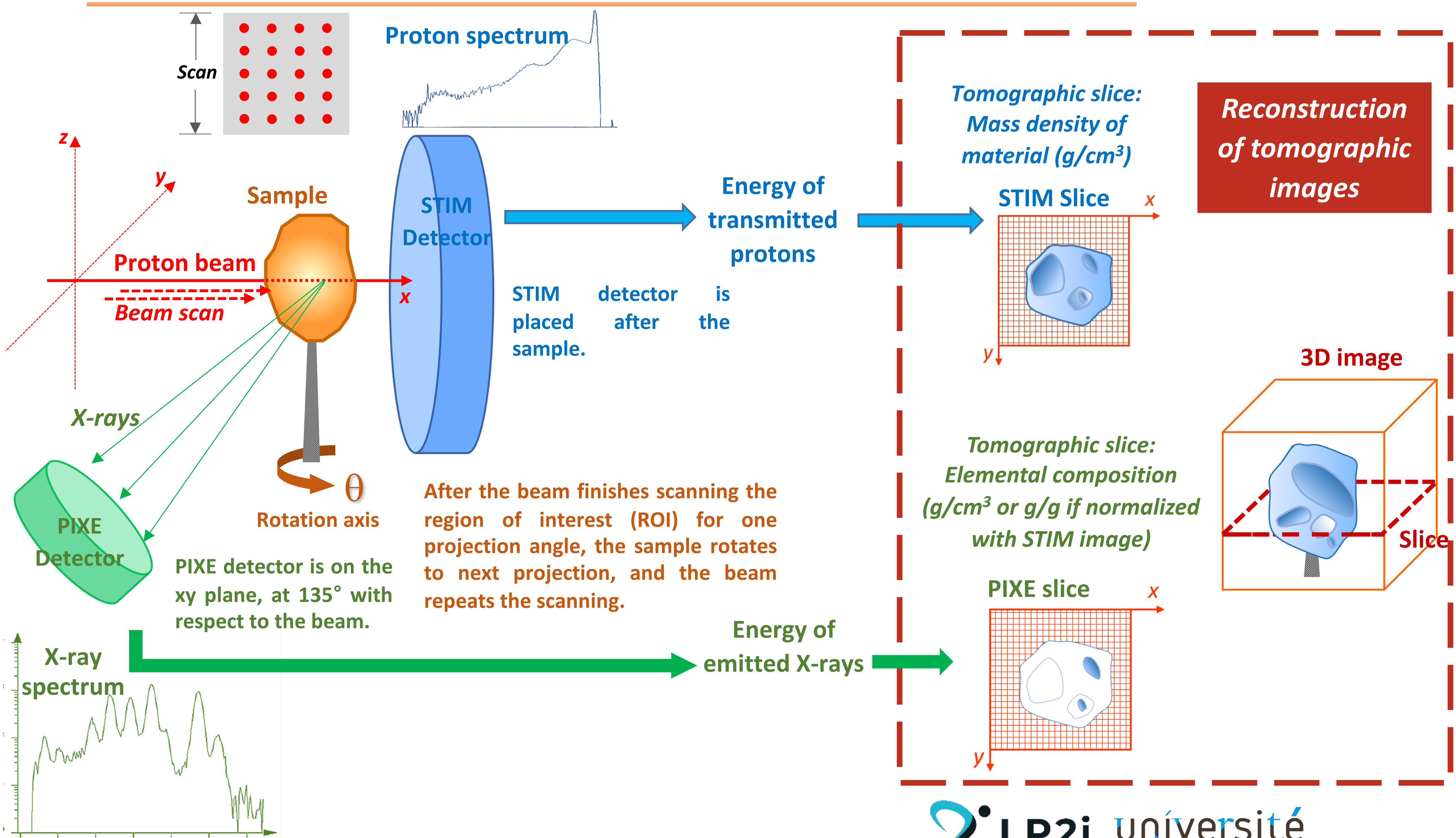
PIXE detector is on the xy plane, at 135° with respect to the beam.

After the beam finishes scanning the region of interest (ROI) for one projection angle, the sample rotates to next projection, and the beam repeats the scanning.

Experimental setup for STIM and PIXE tomography



Experimental setup for STIM and PIXE tomography

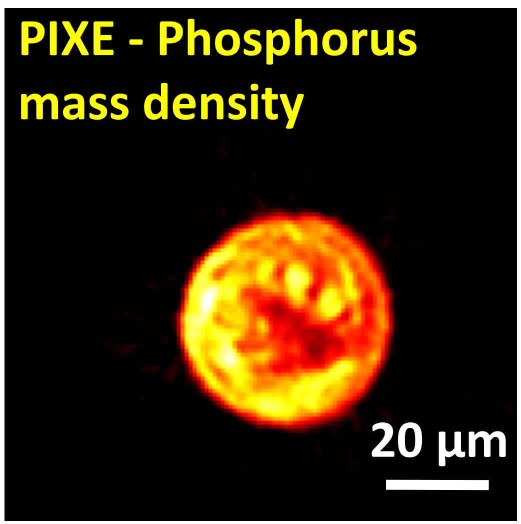


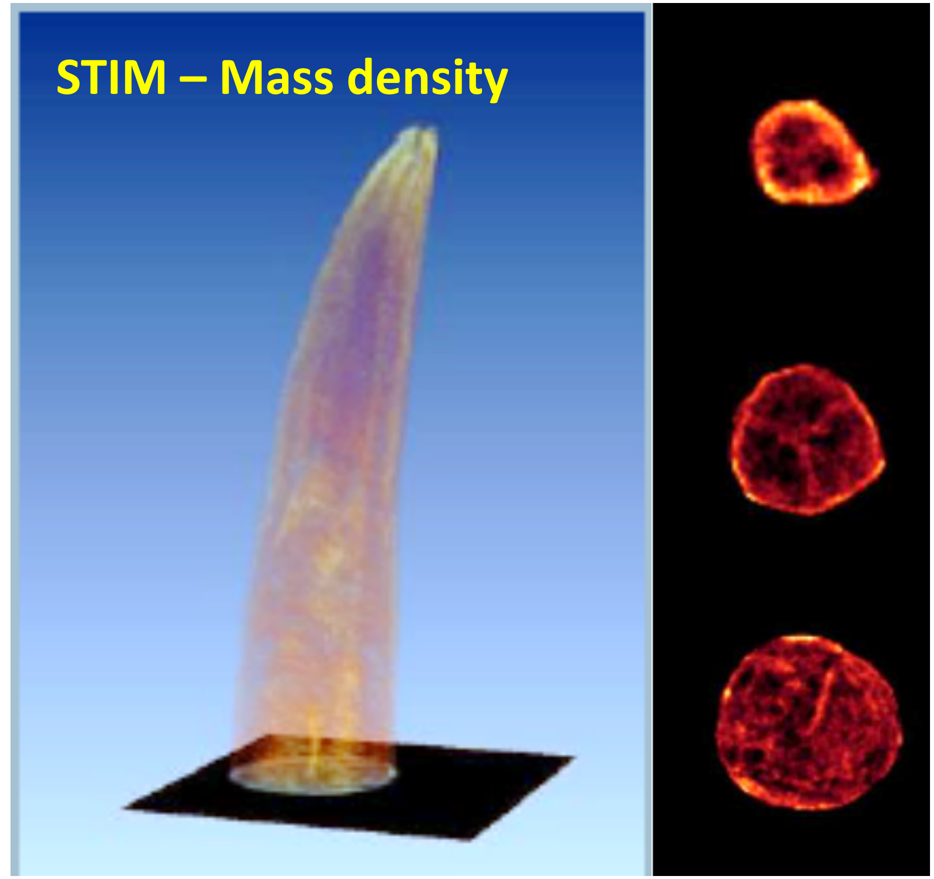
Reconstruction of tomographic images

TomoRebuild: quantitative reconstruction software package, developed at CENBG/LP2IB laboratory.

Reconstruction on STIM tomography data
➔ Distribution of mass density

Reconstruction on PIXE tomography data
➔ Distribution of element mass density





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Example

Objectives:

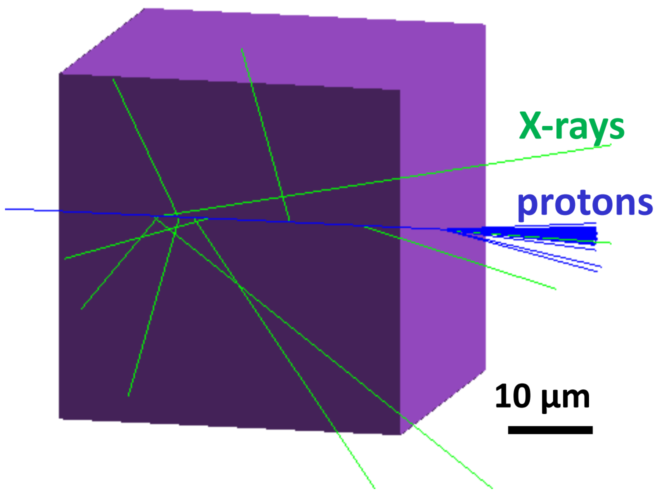
- Simulate STIM and PIXE tomography imaging processes
- Use simulated results as an input to generate tomographic images
- Evaluate the accuracy of tomographic reconstruction methods

Steps:

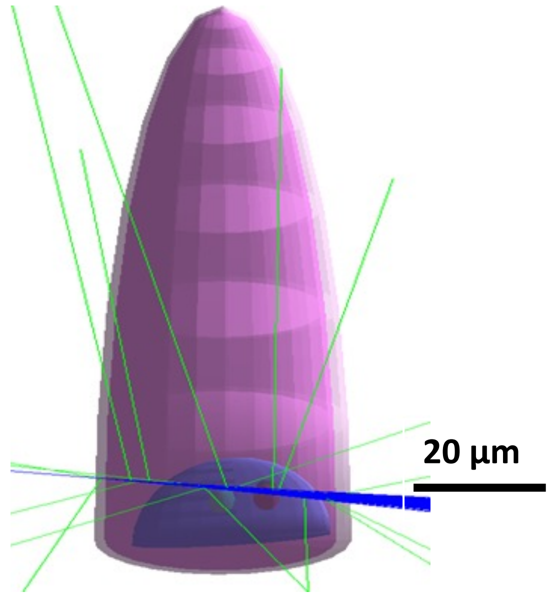
Step 1 - Construct phantoms

Three phantoms are available in the example:

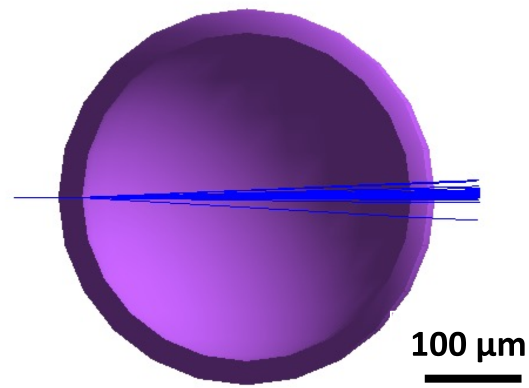
- Homogeneous cube
- Upper part of *C.elegans*
- Inertial confinement fusion target



Simple cube



C. elegans



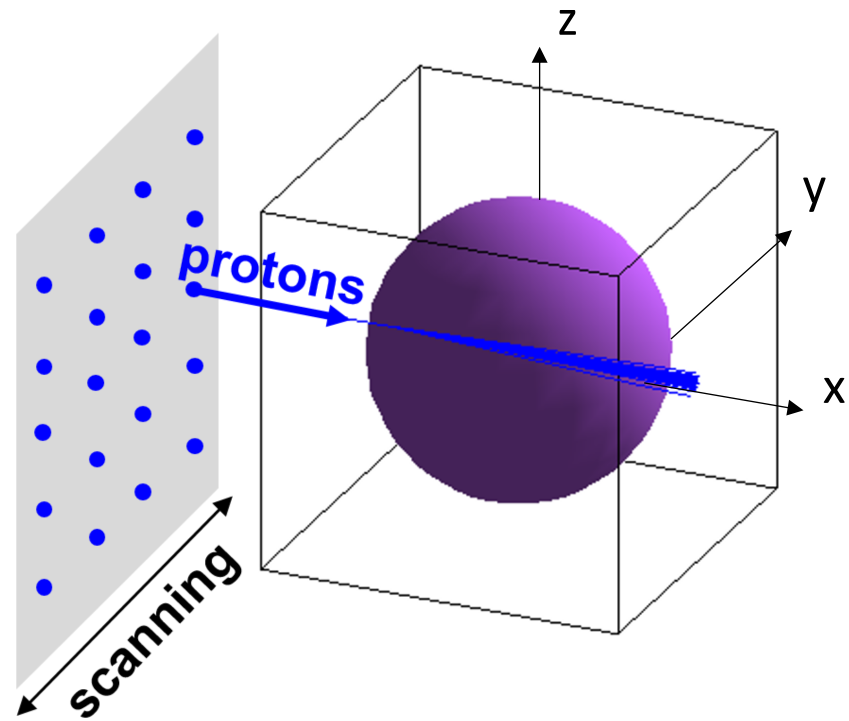
Inertial confinement fusion target

Step 2 - Define simulation parameters

Simulation parameters need to be defined in a *C script*, including:

- Scan size, *i.e.* number of projections, slices, pixels
- Energy
- Production cut (important to reduce the simulation duration)
- Physics list

The *C script* automatically calculates the positions and momentums of the incident beam and generates the *.mac* file that is used to run the simulation



Step 3 - Save the simulated data

❖ **Simulation is long** ➔ **Multithreaded mode**

e.g. using 100 threads:

STIM-T: ~2 hours for 100 projections × 128 slices × 128 pixels

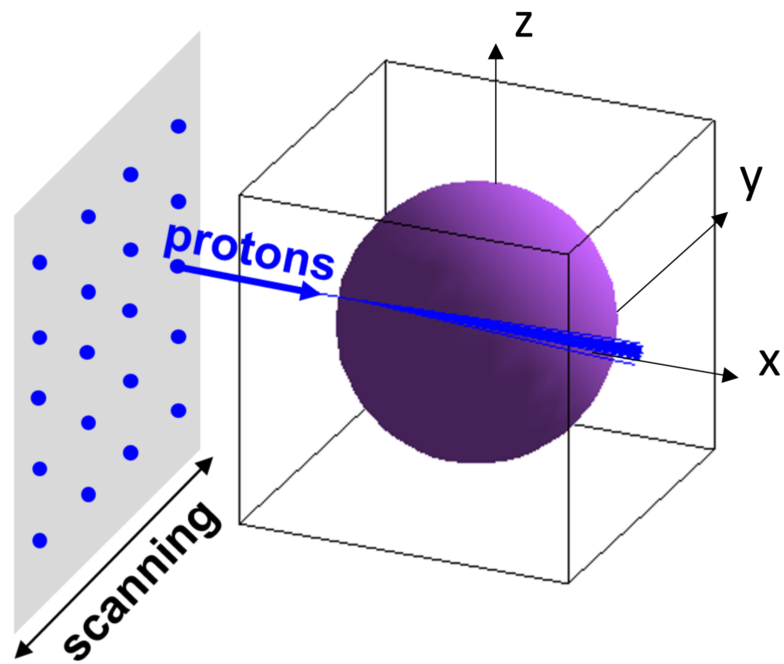
PIXE-T: ~10 days for 100 projections × 1 slice × 128 pixels

❖ **Result data is big:**

e.g. for PIXE-T (100 projections × 1 slice × 128 pixels; 10^6 protons per beam), data includes:

- Energy, momentum of the emitted X-rays
- Index of the projections, slices and pixels of X-rays

❖ **Risks of simulation interruption like power failure…**



➔ **Result data are saved as *struct*, and appended in a binary file (a few Mb per slice).**

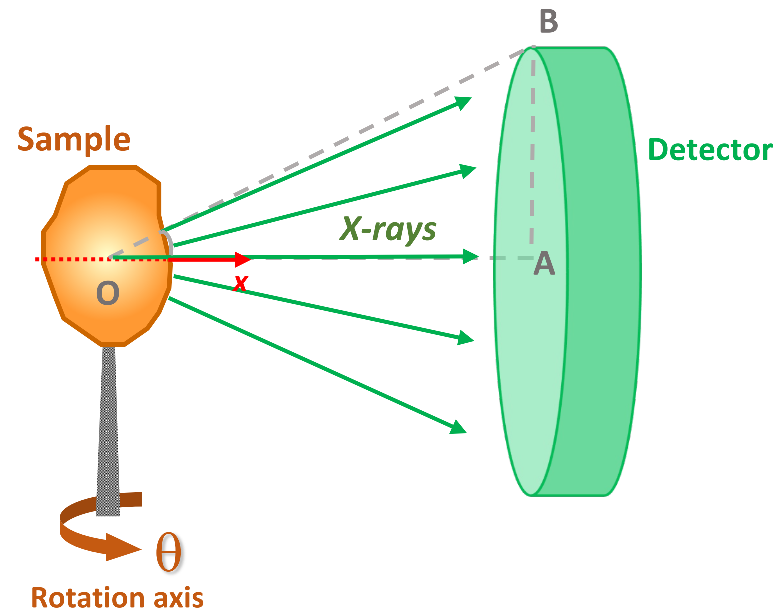
➔ **In case of interruption, we developed a *C script* to locate where the simulation is interrupted and to resume the whole simulation.**

Step 4 – Sort the data to model the detector

We do not want to do the simulation again if we change the angle of position of the PIXE detector.

➔ In the simulation, we record all the particles of interest in 4π. Then we make a selection of the data to model the detector. The selection is performed *after* the simulation by using a *C script* according to two conditions:

- the angular position of the detector with respect to beam direction, *e.g.* 135° for PIXE-T
- the detector solid angle related to $\widehat{AOB}$



A documentation describing the two *C scripts* used for this advanced example will be available:

- the first script to generate the ***.mac*** file
- the second to sort the data to model the detector

Outline

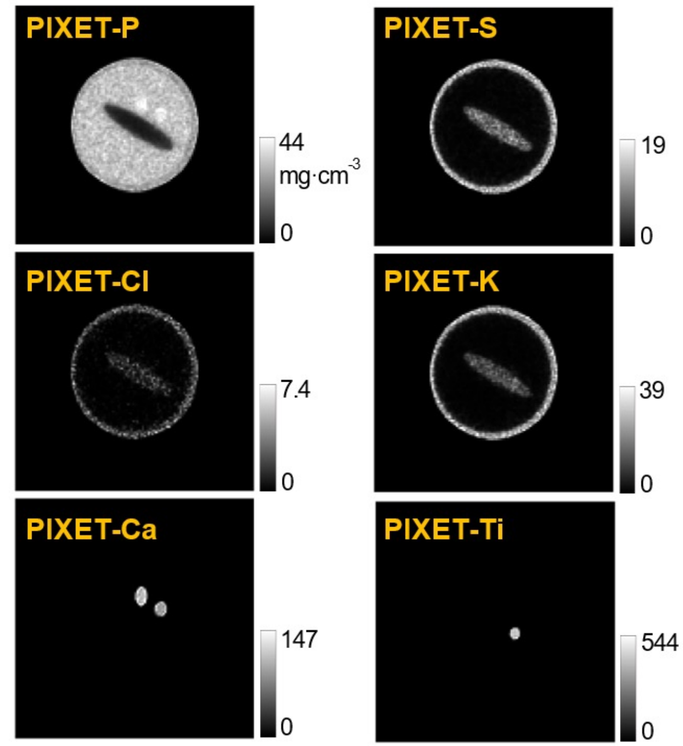
Results

By comparing the quantitative reconstructed images with the reference values, which were set for constructing the phantom, we can evaluate or check the accuracy of reconstruction methods:

e.g. evaluation of two correction methods for X-ray attenuation in TomoRebuild software: ≤ **4% for phosphorus and titanium**

Example for phosphorus and titanium	C. ELEGANS PIXE			
	Average density P (mg/cm^3)	*Relative error*	Average density Ti (mg/cm^3)	*Relative error*
No correction	18.4 ± 1.8	*-38%*	276 ± 22	*-33%*
NLXP correction only	21.5 ± 2.0	*-28%*	374 ± 29	*-8.7%*
XA correction only	26.2 ± 2.4	*-12%*	294 ± 24	*-29%*
Total correction	**30.6 ± 2.7**	***3.7%***	**398 ± 31**	***-2.9%***
Reference value	**29.5**		**409**	

➔ **Implemented reconstruction methods are satisfactory**



Reconstruction of PIXE tomographic slices on *C. elegans*

Michelet C., Li Z. et al. *A Geant4 simulation of X-ray emission for three-dimensional proton imaging of microscopic samples*. Phys Med. 2022;94:85-93

Perspectives

Simulation of classical (2D) imaging

Our example was initially developed for applications in tomographic imaging. However, it is also suited for “classical” (2D) STIM and PIXE imaging. Thus, it could be used to check the accuracy of quantitative 2D imaging.

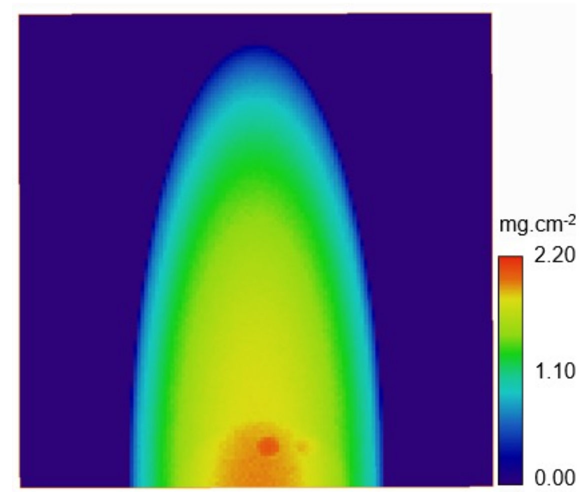
Using ion or X-ray beam

The type and energy of incident particles are defined in ***.mac*** file used to run the code, they are very easy to modify. So any source can be used, *e.g.* ion or X-ray beam.

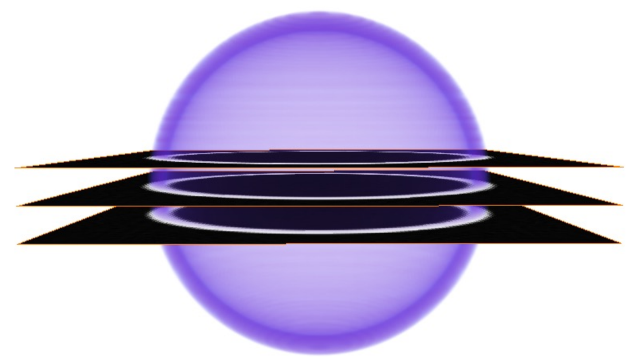
Work in progress:

Simulation of proton tomography imaging on an inertial confinement fusion target (ICF), in collaboration with H. Shen, Fudan University, Shanghai

Released soon



2D scan of the *C. elegans* phantom



3D image of STIM tomography of ICF