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Acceleration of 3D reconstruction in cryo-EM

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Visualization of Molecules

Several methods are able to visualize molecules on atomic level

- X-ray diffraction
- nuclear magnetic resonance (NMR)
- cryo-electron microscopy (cryo-EM)

Cryo-EM has some superiority over other methods

- catches molecules in natural environment (diffraction needs crystalization)
- usable for large molecules (NMR is restricted to smaller proteins)

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Cryo-electron microscopy

Rapidly-developed recently

- in 2012, there was only four structures at near-atomic resolution
- in 2015, 115 structures was discovered
- this progress is allowed by direct electron detectors, viterious ice and **image reconstruction methods**

In 2017, Nobel price in chemistry was given for cryo-EM

- Jacques Dubochet, Joachim Frank, Richard Henderson
- Joachim Frank got his price for image processing methods allowing to obtain 3D structure from electron microscope data

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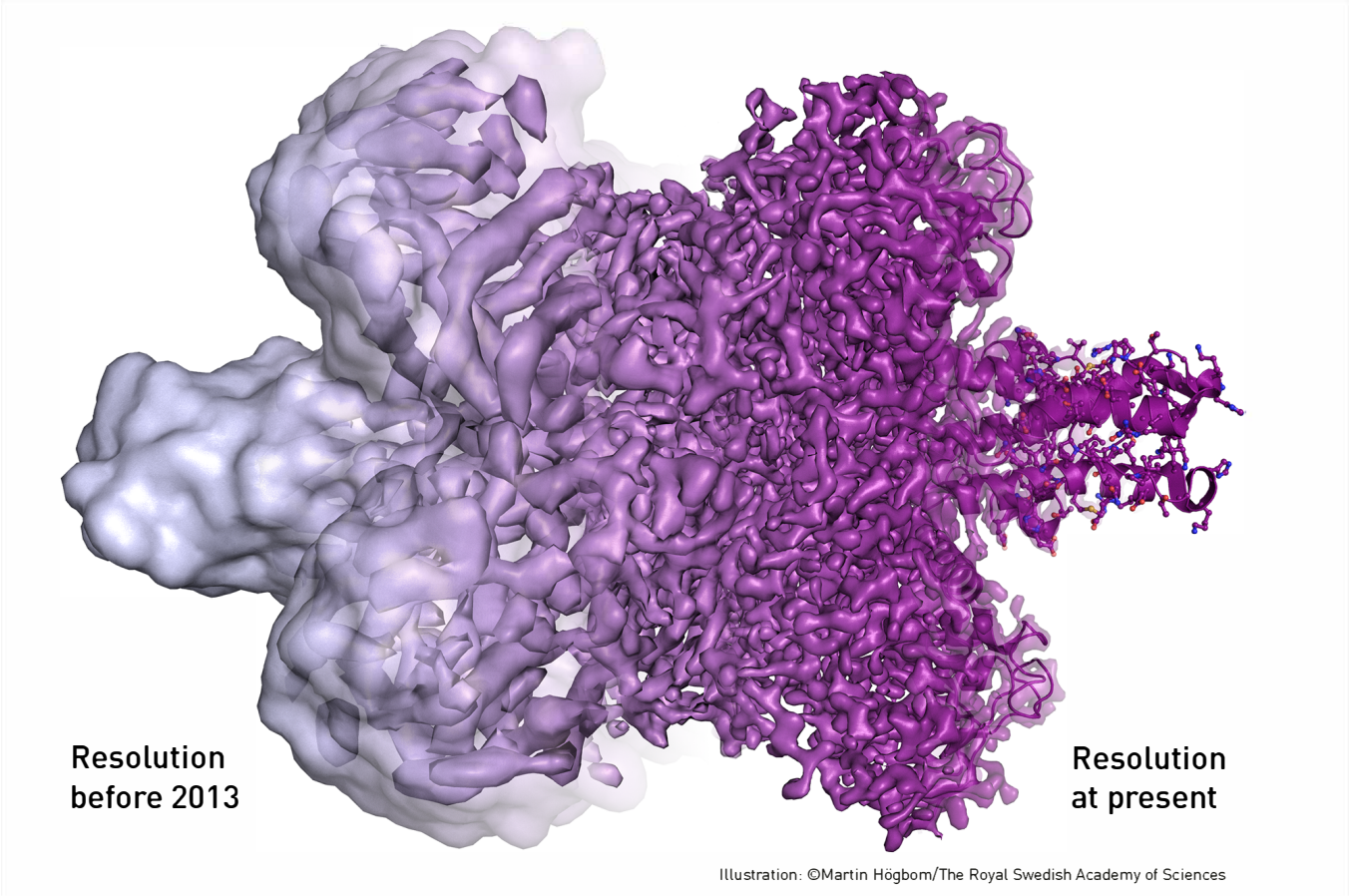
Cryo-electron microscopy



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Specimens in the Ice

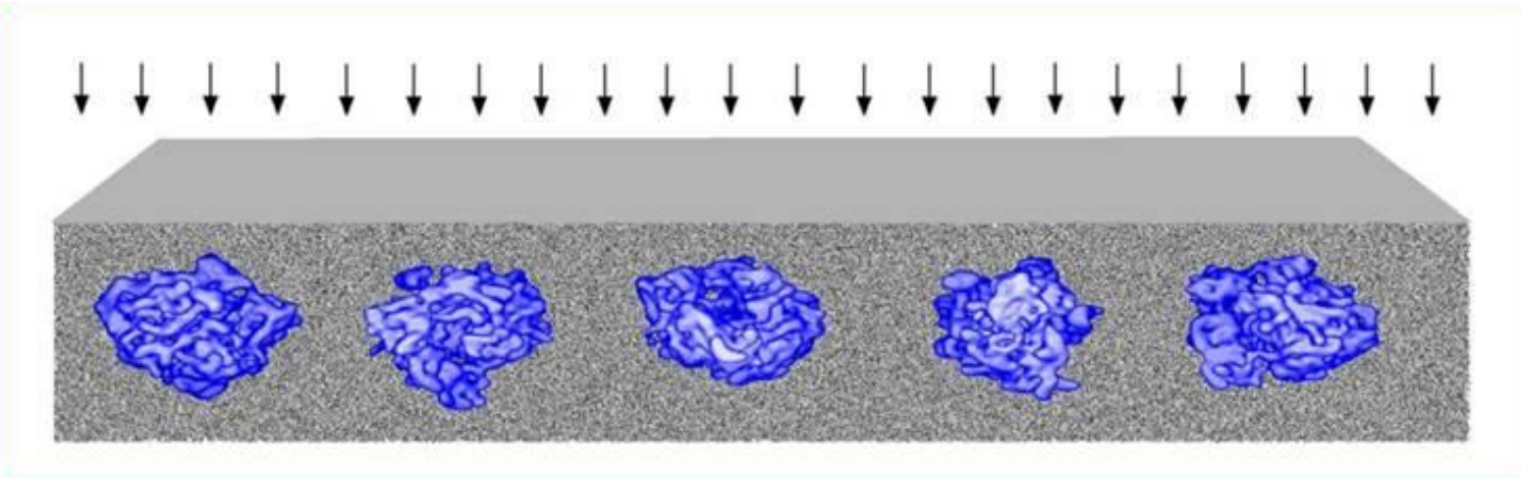

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Image Analysis in Cryo-EM

Reconstruction of 3D volume is challenging

- electron beam causes damages, so it must be weak, so a noise-to-signal distance is very low
- surrounding water adds another source of noise
- specimens are captured in random positions, possibly with conformational changes
- when captured multiple times, the image is moving and deforming

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Raw data from microscope

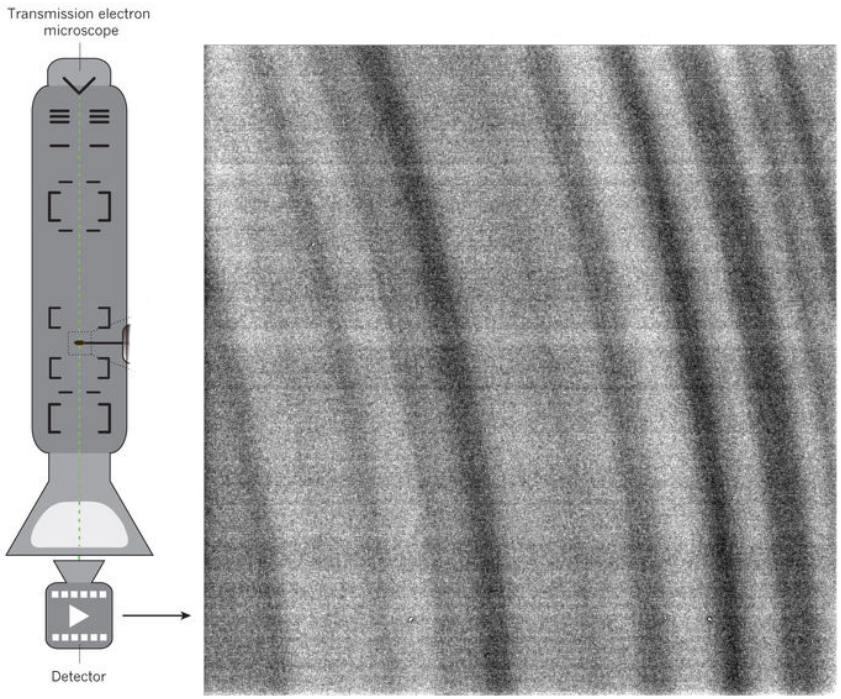

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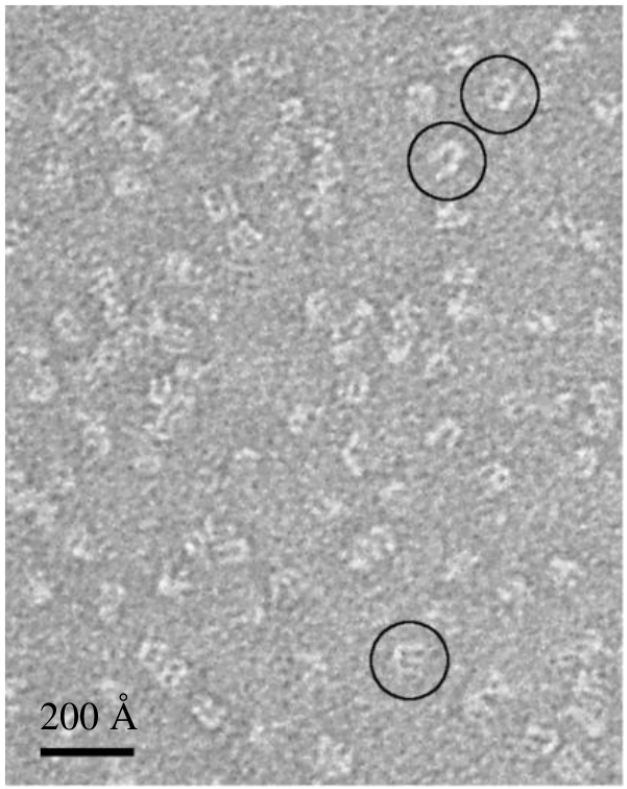
Image of Specimens



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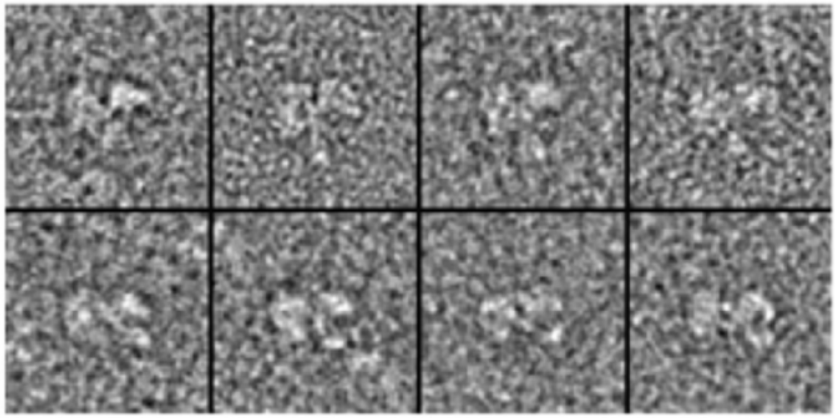
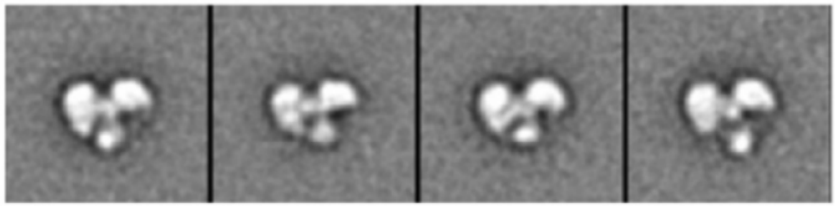
Aligning Images





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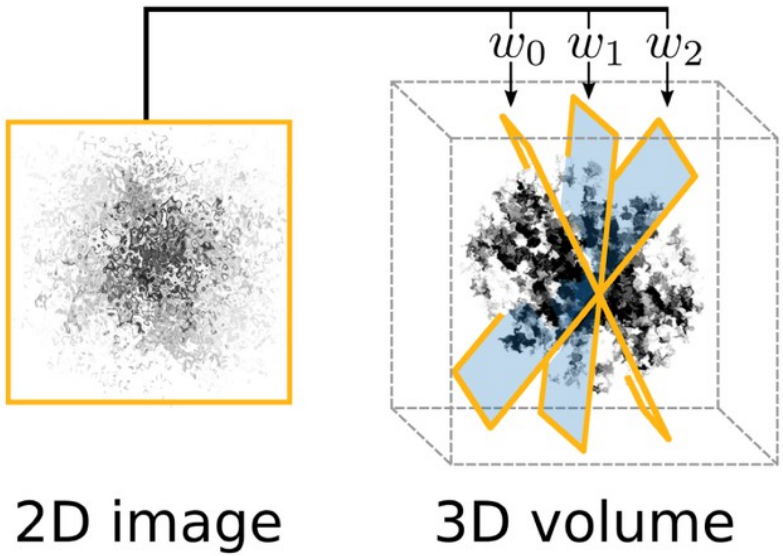
3D Volume Reconstruction



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Our Focus

Image reconstruction is very computationally-demanding

- requires thousands of CPU hours at least
- 3D reconstruction is one of main bottlenecks

We focus on acceleration of 3D volume reconstruction in Xmipp software

- software developed in Spanish National Center for Biotechnology (CNB-CSIC)
- production use, not a prototype-toy

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Getting 3D Volume from Images?

Central slice theorem

- let i be real-space projection image, which has concentrated information about 3D volume v
- let I be a Fourier transform of image i and V be Fourier transform of v
- I forms a slice of V with the same orientation as i holds with respect to v, moreover, slice I is going through center of V

So, we need to transform our images into Fourier space, create 3D Fourier volume and transform the volume back to real space.

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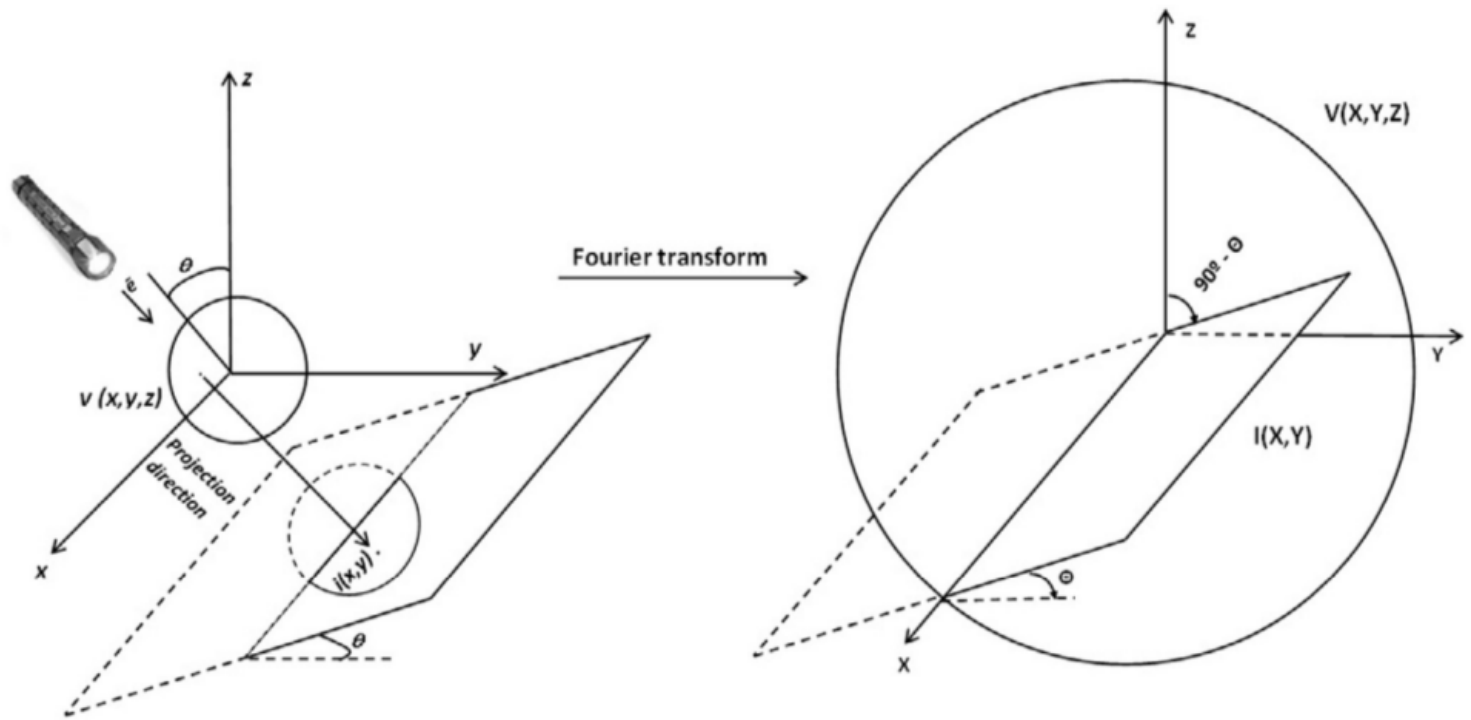
3D Volume Reconstruction



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3D Volume Reconstruction

We need to guess orientation of each 2D image

- computed iteratively
- bottleneck is creating 3D volume from 2D images

We have accelerated the creation of 3D volume on GPUs.

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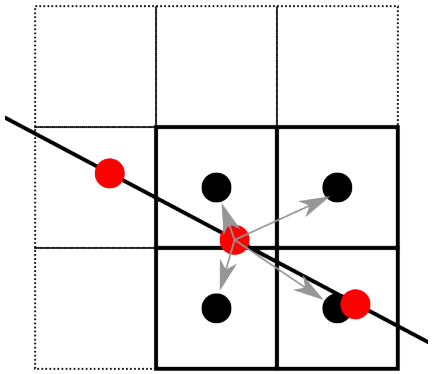
State-of-the-art

Multiple papers deal with GPU acceleration of 3D reconstruction, all implementing a scatter method

- GPU thread are associated to 2D pixels of the image
- each thread computes projection of the pixel into volume (resulting in floating-point position)
- the pixel value is put into multiple voxels (integer position) using interpolation



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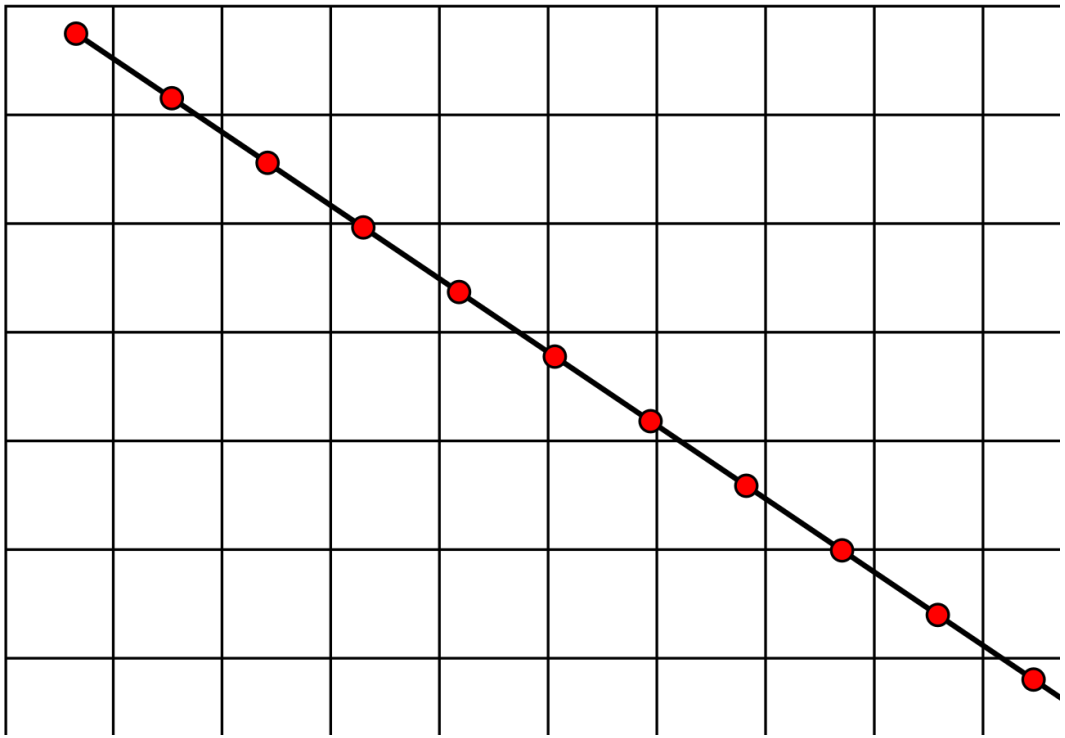
State-of-the-art



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State-of-the-art

Drawbacks of scatter pattern

- race conditions in writing (distances within a voxel up to $\sqrt{3}\times$ longer than distance between two pixels), requires atomic writes
- some wrong optimizations removing atomics have been published
- frequent writing into 3D domain with poor spatial locality

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The Gather Pattern

The image value is computed for each 3D voxel

- so each voxel is written only once
  - no race conditions in reading
- image data are interpolated (we obtain floating-point position in the image), so they are accessed multiple times
  - much better memory locality (we are now repeating accesses into 2D image, not 3D volume)

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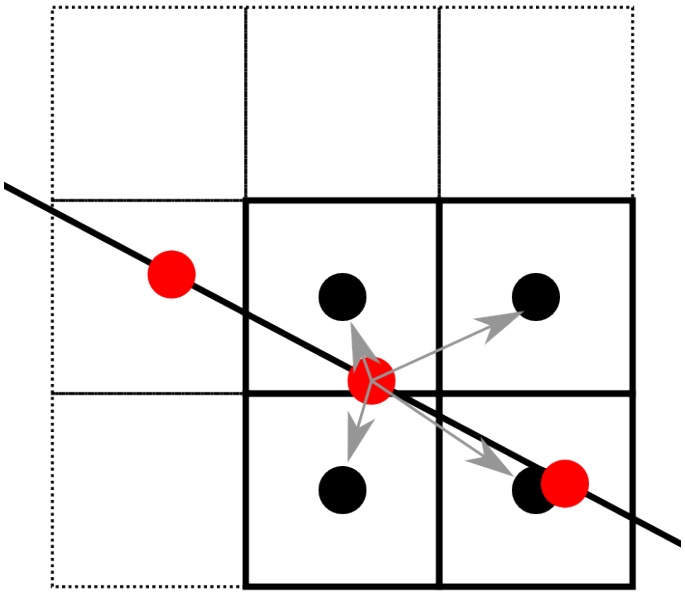
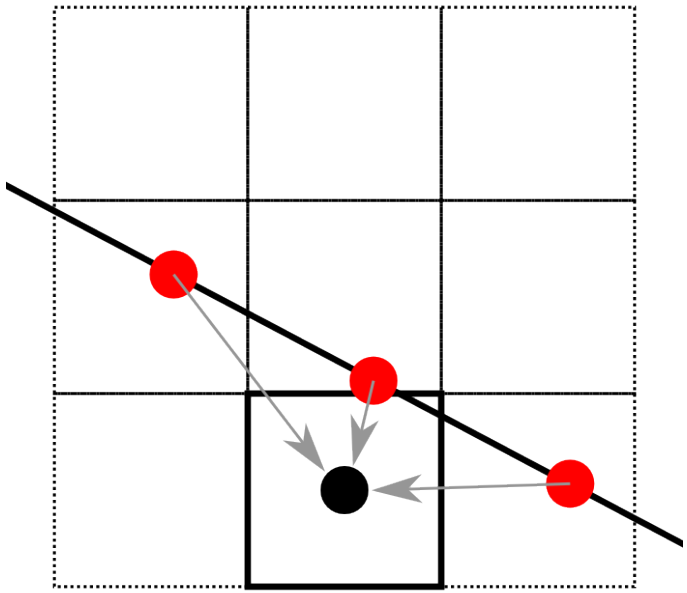
The Gather Pattern





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The Gather Pattern

Projecting 3D voxels to 2D image

- when going into image space, we get position in the image and z-distance from the image
- a lot of voxels do not hit the image (z-distance is too high, or they are out of image boundaries)
  - we have $\mathcal{O}(n^2)$ pixels, but $\mathcal{O}(n^3)$ voxels – a lot of them is not used

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The Gather Pattern

Projection planes optimization

- we look at the image from some plane orthogonal to coordinate axes (XY, XZ, YZ), which maximizes projected image size
- the iteration space is reduced to the projection plane
- for each point of the projection plane, we compute the distance of the image and start to process voxels from there

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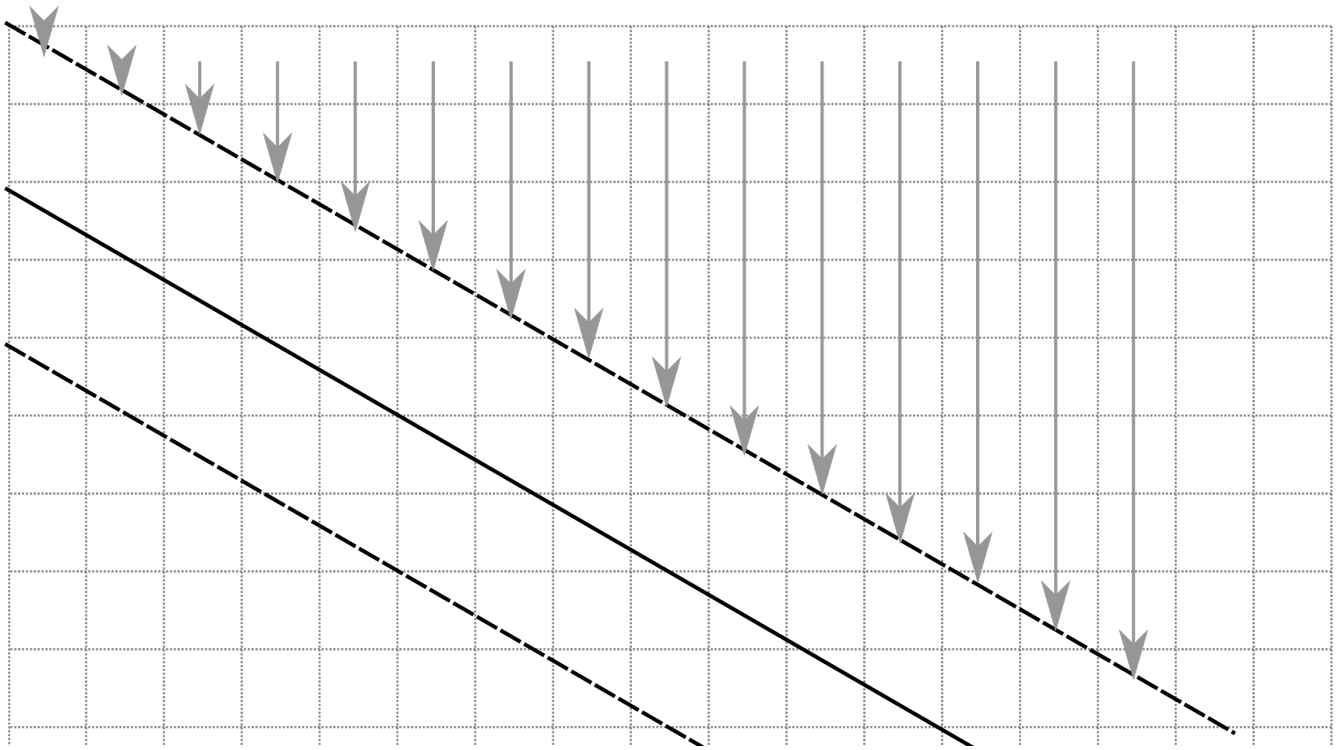
The Gather Pattern



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Basic GPU Implementation

The gather pattern can be rewritten for GPU directly

- one GPU thread is assigned to one point of projection plane

Optimization opportunities

- the advanced interpolation method may be computationally demanding
- GPU cache system is limited in maintaining data locality

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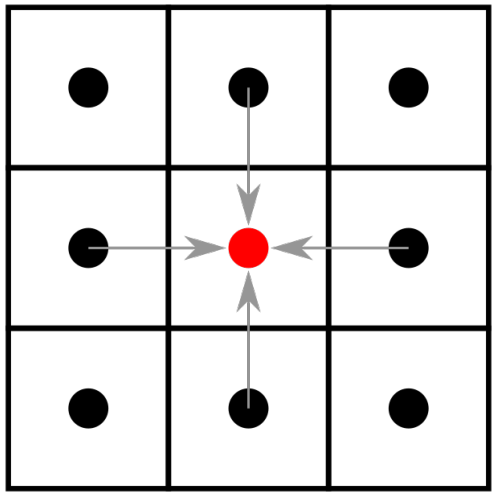
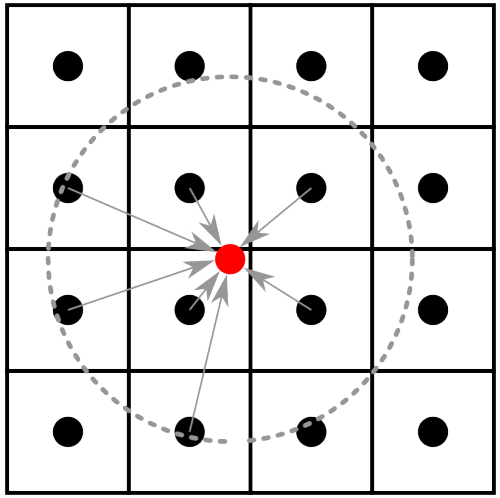
Interpolation

Our computation is a kind of stencil, but with floating-point positions

- interpolation coefficients cannot be precomputed easily





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Interpolation

We have implemented two strategies

- on-the-fly interpolation
- precomputed table for very fine steps (originally in Xmipp)
  - can be cached or preloaded into shared memory

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Explicit Caching of Image Data

A thread block accesses only a part of the image

- can be cached in fast shared memory
- however, its size may vary depending on image rotation
  - we upper-bound image size to $\lceil \sqrt{2}\sqrt{3}(b + 2i) \rceil$, where b is thread block size and i is interpolation radius
  - shared memory is allocated to upper-bound prior GPU kernel execution
- for each image, AABB is computed and proper size is preloaded in shared memory

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Additional Optimizations

Register consumption optimization

- many parameters into templates or macros
- allows to increase GPU parallelism

CPU-GPU load balancing

- CPU prepares images for GPU, one core is not powerful to do so
- multiple threads are preparing images and sharing GPU time, also allows copy and computation overlay

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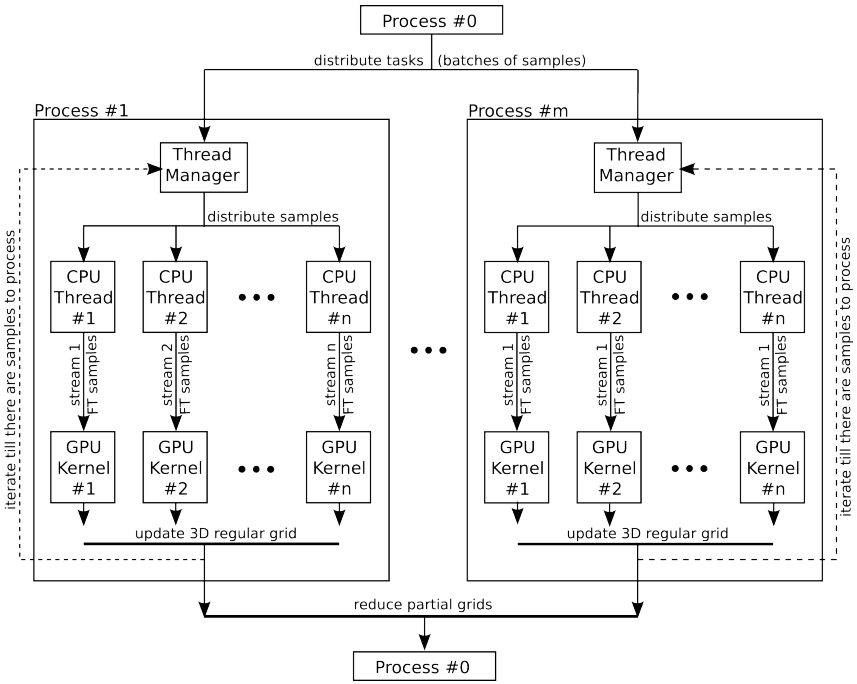
Architecture



Obrázek: Architecture of 3D Fourier Reconstruction.

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Autotuning

parameter	values
BLOCK_DIM	8, 12, 16, 20, 24, 28, 32
ATOMICS	0, 1
GRID_DIM_Z	1, 4, 8, 16
PRECOMP_INT	0, 1
SHARED_INT	0, 1
SHARED_IMG	0, 1
TILE_SIZE	1, 2, 4, 8

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Evaluation

Tested on a GPGPU cluster node

Processor	performance	memory BW
2× Xeon E5-2650 v4	845 GFlops	154 GB/s
1× Tesla P100	9,519 TFlops	732 GB/s
4× Tesla P100	38,076 TFlops	2928 GB/s
theoretical speedup (1 GPU)	11.3×	4.75×

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Evaluation

execution	time	speedup over original
2× CPU	155m	n/a
1× GPU	13m35s	11.4×
4× GPU	4m53s	31.7×

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Performance Portability

Tabulka: Performance portability of 3D Fourier Reconstruction

	P100	GTX1070	GTX750	GTX680
Tesla P100	100%	95%	44%	96%
GTX 1070	88%	100%	31%	50%
GTX 750	65%	67%	100%	94%
GTX 680	71%	72%	71%	100%

We can gain over 3× speedup when tuning for each GPU architecture.

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Performance Portability

Tabulka: Sensitivity on input images in 3D Fourier Reconstruction (GTX 1070)

	128x128	91x91	64x64	50x50	32x32
128x128	100%	100%	77%	70%	32%
91x91	100%	100%	76%	68%	33%
64x64	94%	94%	100%	91%	67%
50x50	79%	78%	98%	100%	86%
32x32	65%	67%	80%	92%	100%

We can gain over 3× speedup when tuning for specific input size.

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Conclusion

We have implemented fast, production-ready algorithm

- significant performance boost
- implemented in Xmipp from beginning

Advantages over state-of-the-art

- gather approach is already significantly faster (about 2x on Pascal architecture)
- we suppose it will be even faster with further architectures (bigger flops-to-memory gap, higher parallelism)
- we do not rely on HW implementation of atomics (negligible slowdown when e.g. result is stored in double-precision)

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Programming Complexity

The basic idea of the algorithm is pretty simple

- we are just putting 2D slices into 3D space, right?

Indexing hell

- Fourier space is symmetric, we need to deal with its boundaries
- going from 3D integer position to 2D real position with handling of 3D symmetry, 2D symmetry and space padding in both 3D and 2D is challenging
- because of real position, it is not always clear if we compute correctly (e.g. how to trace boundary conditions?)
- the indexed space is extremely large
- gnuplot seems really good tool

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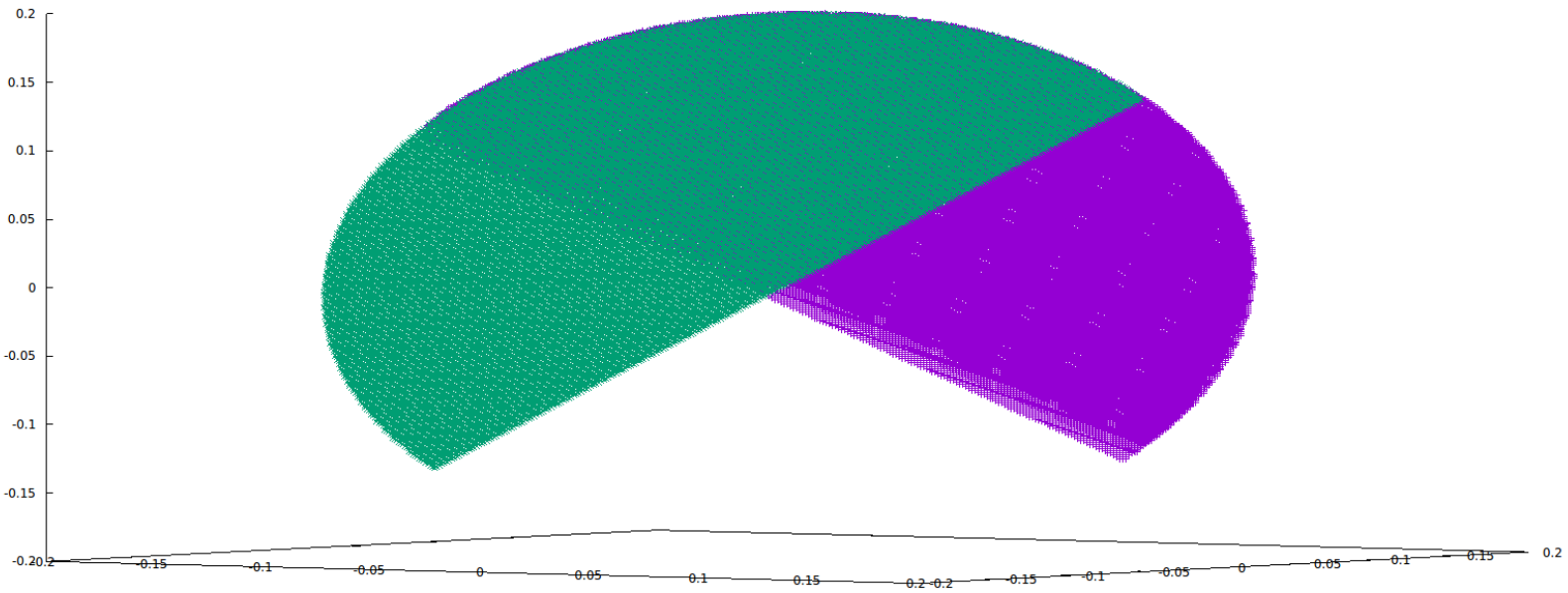
Debuging with gnuplot



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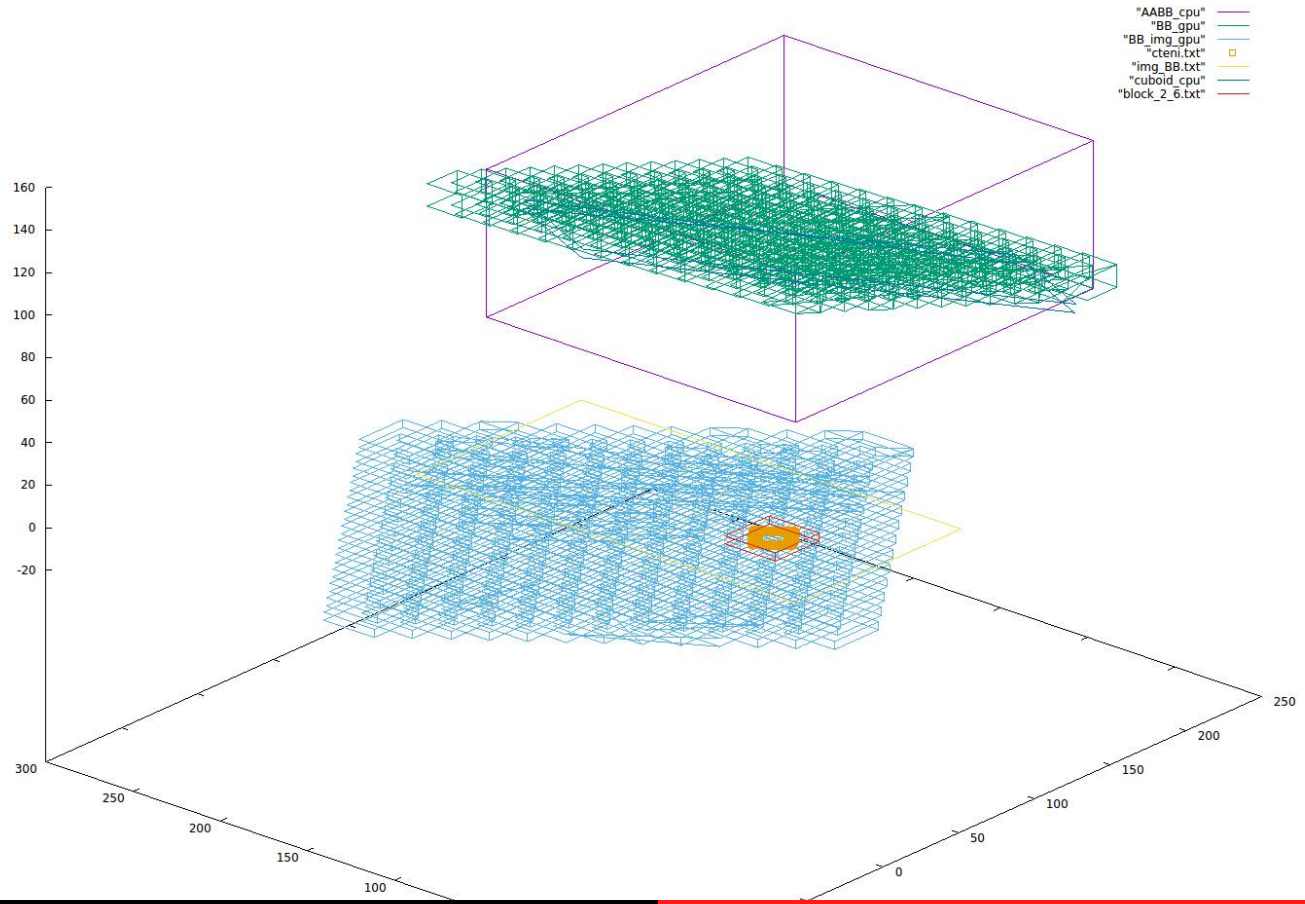
Debuging with gnuplot



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Finding Bugs

It is not simple to determine what is a bug in noisy data

- just by moving from scatter to gather, we already compute something else

Errors in some part of pipeline are difficult to interpret

- e.g., bad indexing in Fourier space looks really weird in real space
- too long chain: 2D real $\rightarrow$ 2D Fourier $\rightarrow$ 3D Fourier $\rightarrow$ 3D real

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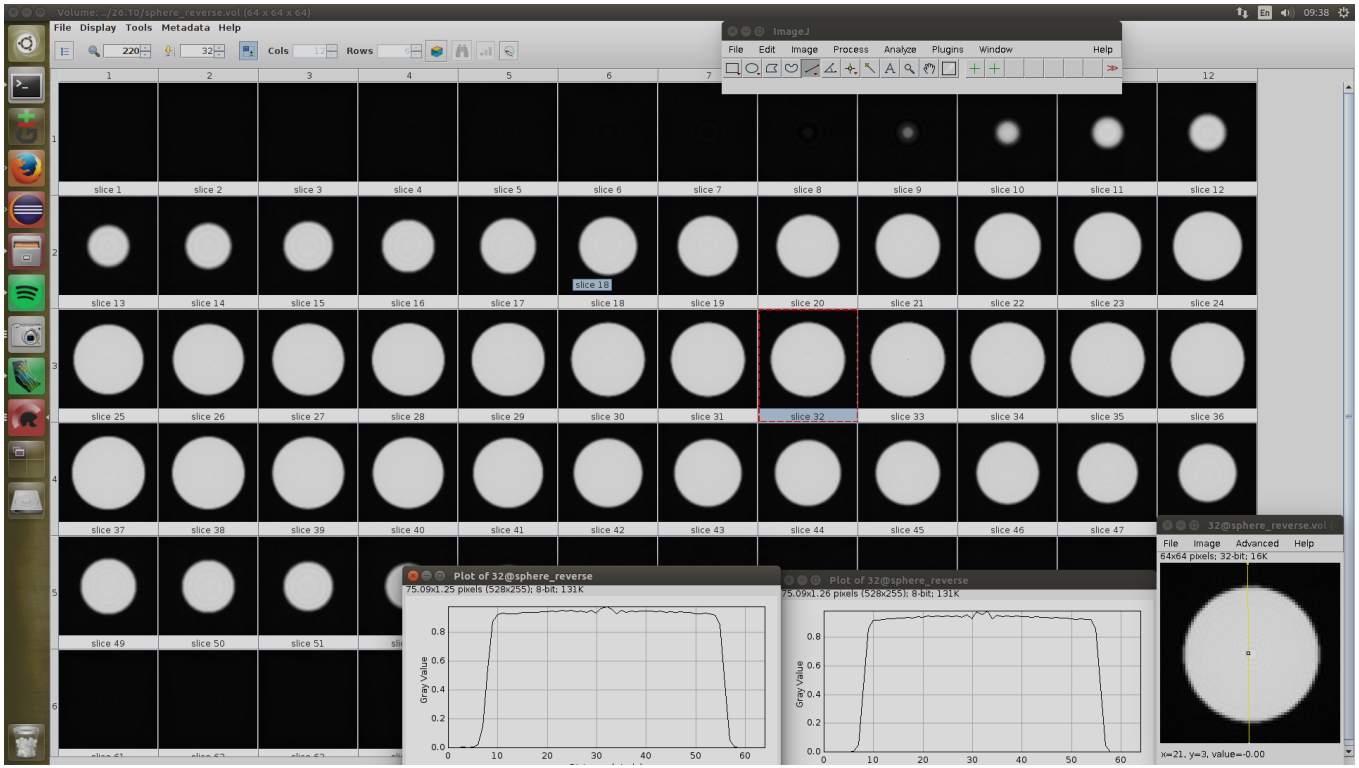
Sphere



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Sphere with Indexing Bug