3-D Reconstruction Algorithms
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Tomography
historical background

- 1956 - Bracewell reconstructed sun spots from multiple views of the Sun from the Earth.

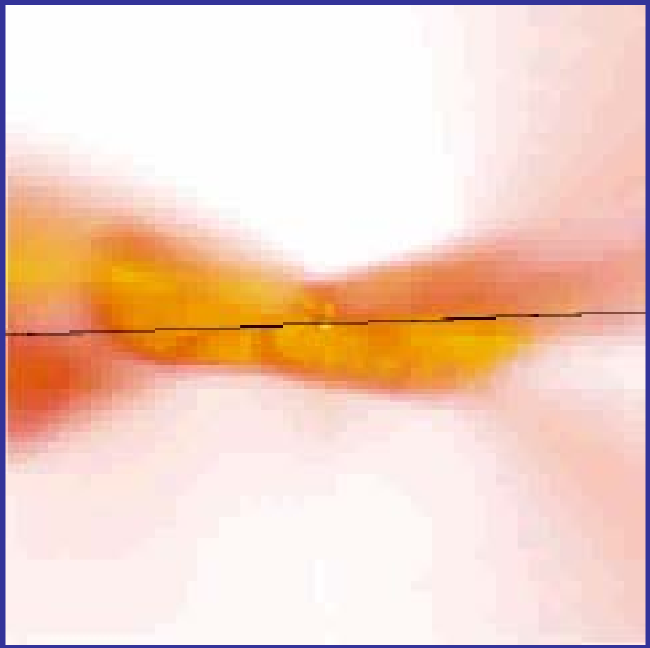
- 1967 - Medical Research Council Laboratory, Cambridge, England: Aaron Klug and grad student David DeRosier reconstructed three-dimensional structures of viruses.

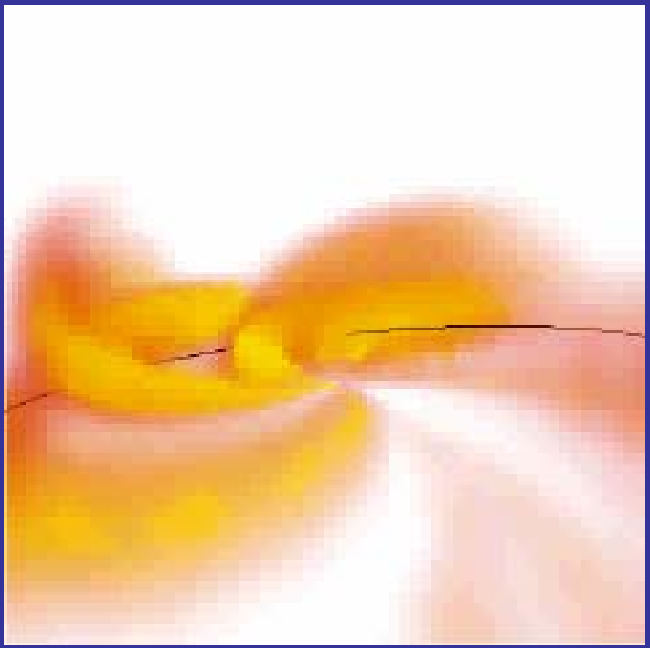
- 1972 - British engineer Godfrey Hounsfield of EMI Laboratories, England, and independently South African born physicist Allan Cormack of Tufts University, Massachusetts, invented CAT (Computed Axial Tomography) scanner. Tomography is from the Greek word *tomos* meaning "slice" or "section" and *graphia* meaning "describing".

- 1977 – W. Hoppe (Germany) proposed three-dimensional high resolution electron microscopy of non-periodic biological structures (single particle reconstruction).

Inner heliospheric plasma density

(to 1.5 times the distance of the Earth from the Sun).

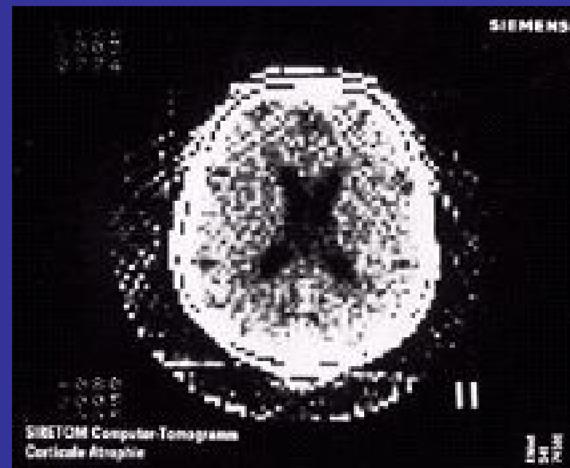




CT scan

Original "Siretom" dedicated head CT scanner, circa 1974.

The first clinical CT scanners were installed between 1974 and 1976. The original systems were dedicated to head imaging only, but "whole body“ systems with larger patient openings became available in 1976. CT became widely available by about 1980. There are now about 6,000 CT scanners installed in the U.S. and about 30,000 installed worldwide.



Original axial CT image from the dedicated Siretom CT scanner, circa 1975.

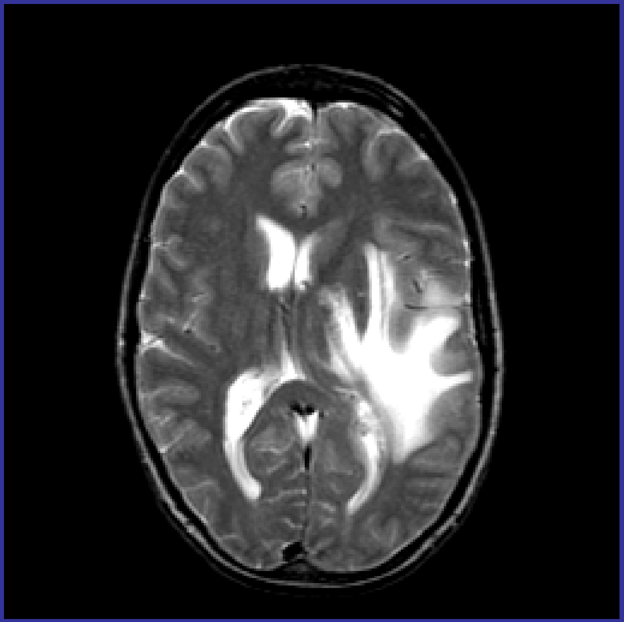
This image is a coarse 128 x 128 matrix; however, in 1975 physicians were fascinated by the ability to see the soft tissue structures of the brain, including the black ventricles for the first time (enlarged in this patient) (Courtesy: Siemens)

Axial CT image of a normal brain using a state-of-the-art CT system and a 512 x 512 matrix image.

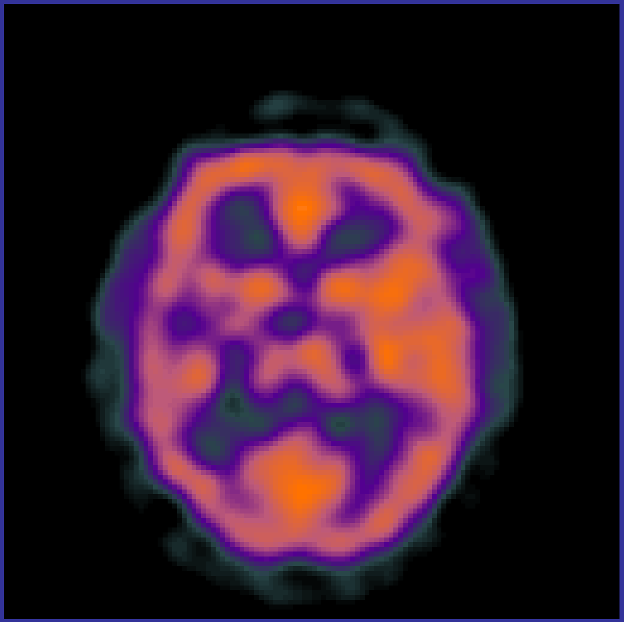
Note the two black “pea-shaped" ventricles in the middle of the brain and the subtle delineation of gray and white matter. (Courtesy: Siemens)

Various physical effects can be used to visualize different aspects of the human body physiology

X-rays



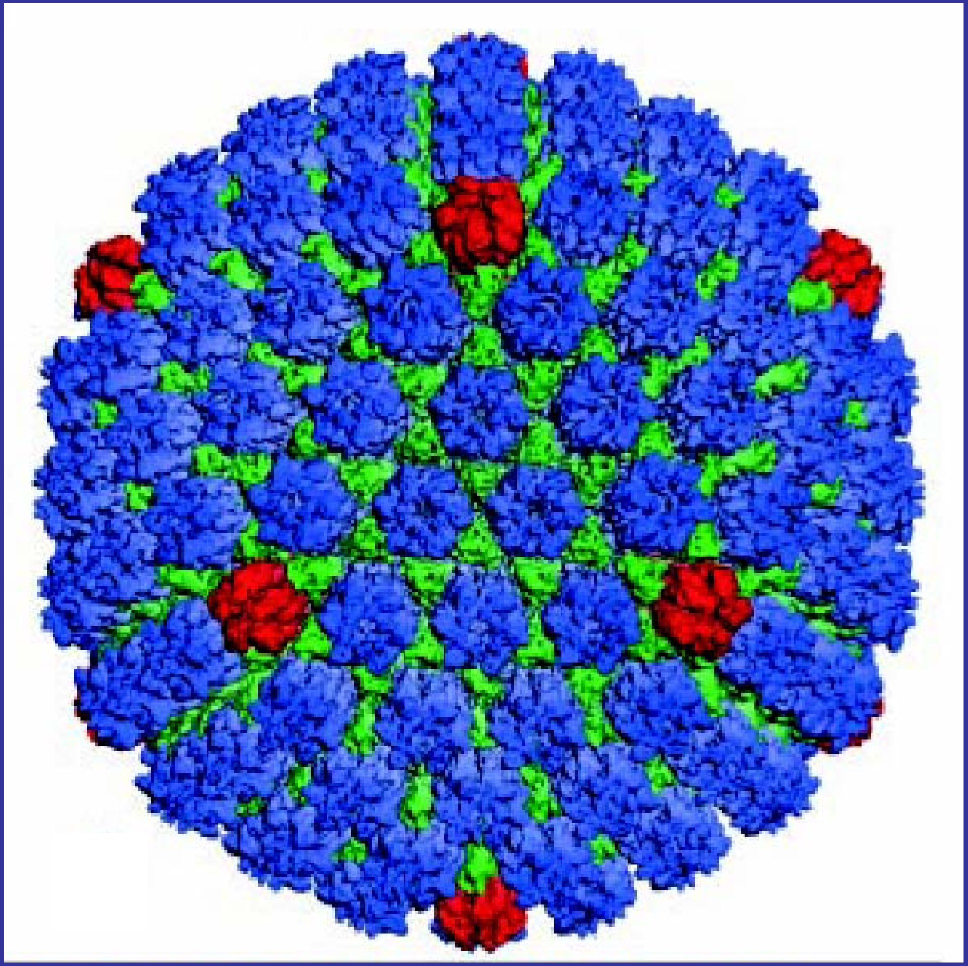
NMR
Nuclear Magnetic Resonance

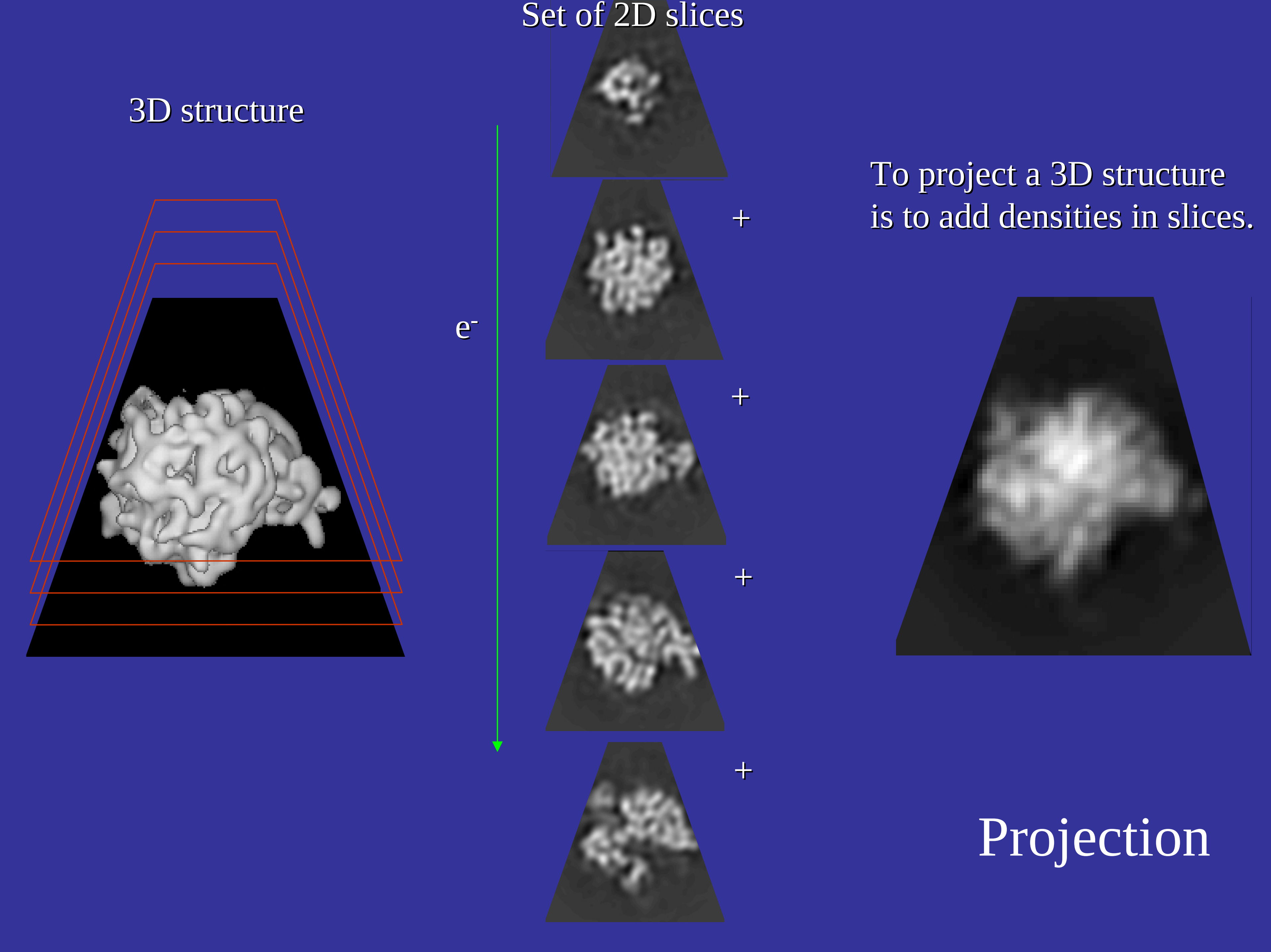


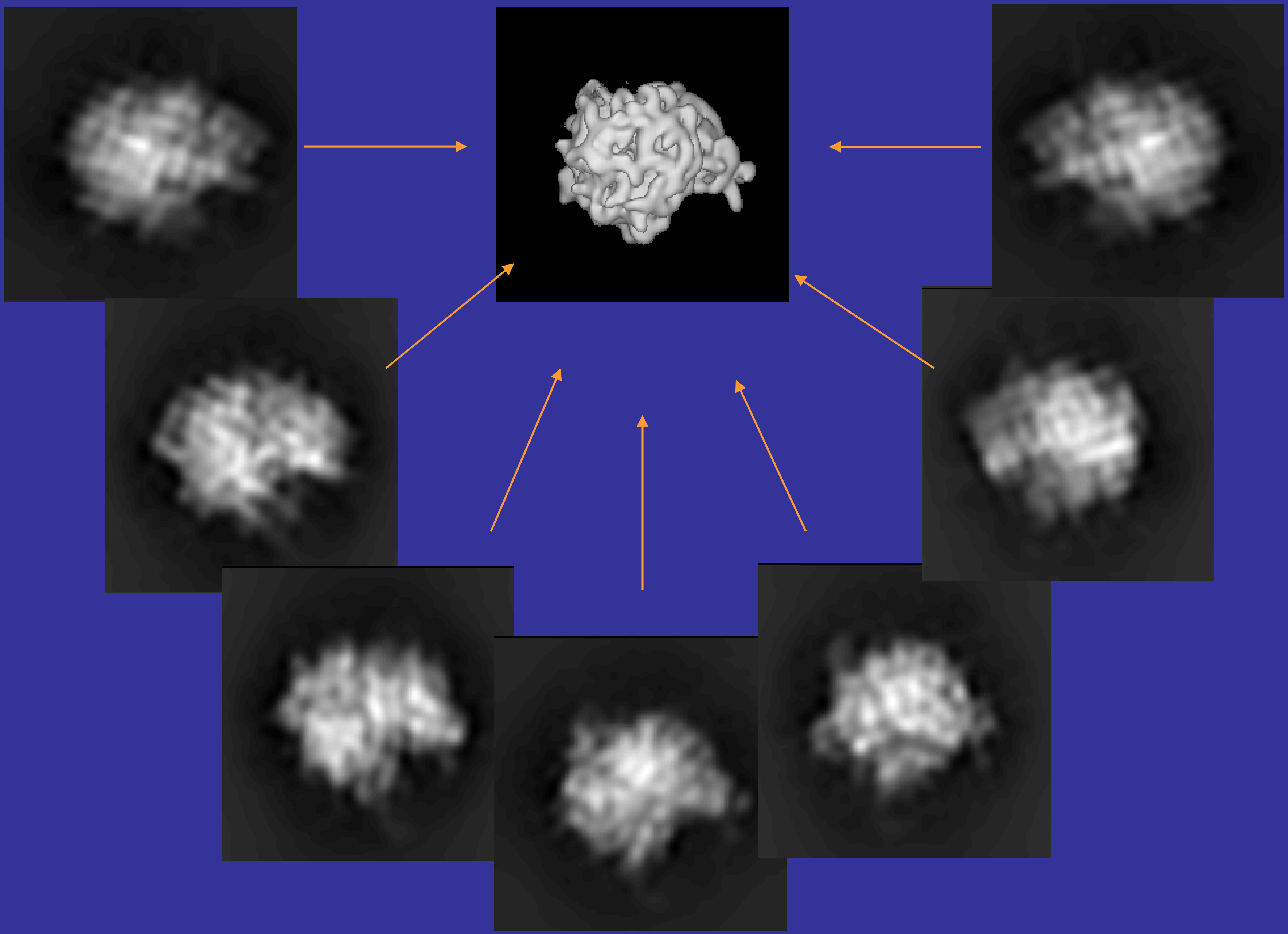
PET
Positron Emission Tomography

Herpesvirus at 8.5 Å resolution

Zhou, Z. H., Dougherty, M., Jakana, J., He, J., Rixon, F. J. and Chiu, W. (2000) Seeing the herpesvirus capsid at 8.5 Å. *Science* **288**, 877-80.

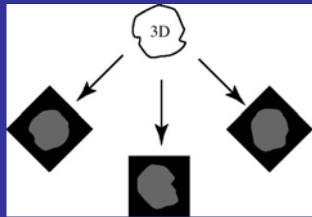



Set of 2D slices
3D structure
To project a 3D structure
is to add densities in slices.
e-
+
+
+
+
Projection

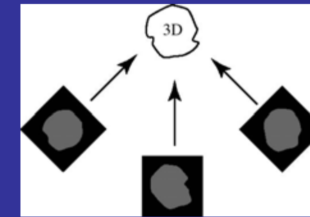


3D reconstruction(Back Projection)

Full range



Mechanism of projection-backprojection



0
1
0

←

0	0	0
0	1	0
0	0	0

↓

0	1	0

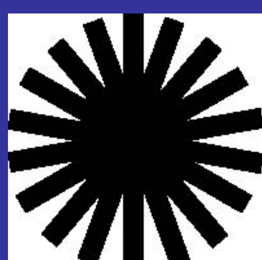
0
1
0

→

0	1	0
1	2	1
0	1	0

↑

0	1	0



r^* weighting

-1
1
-1

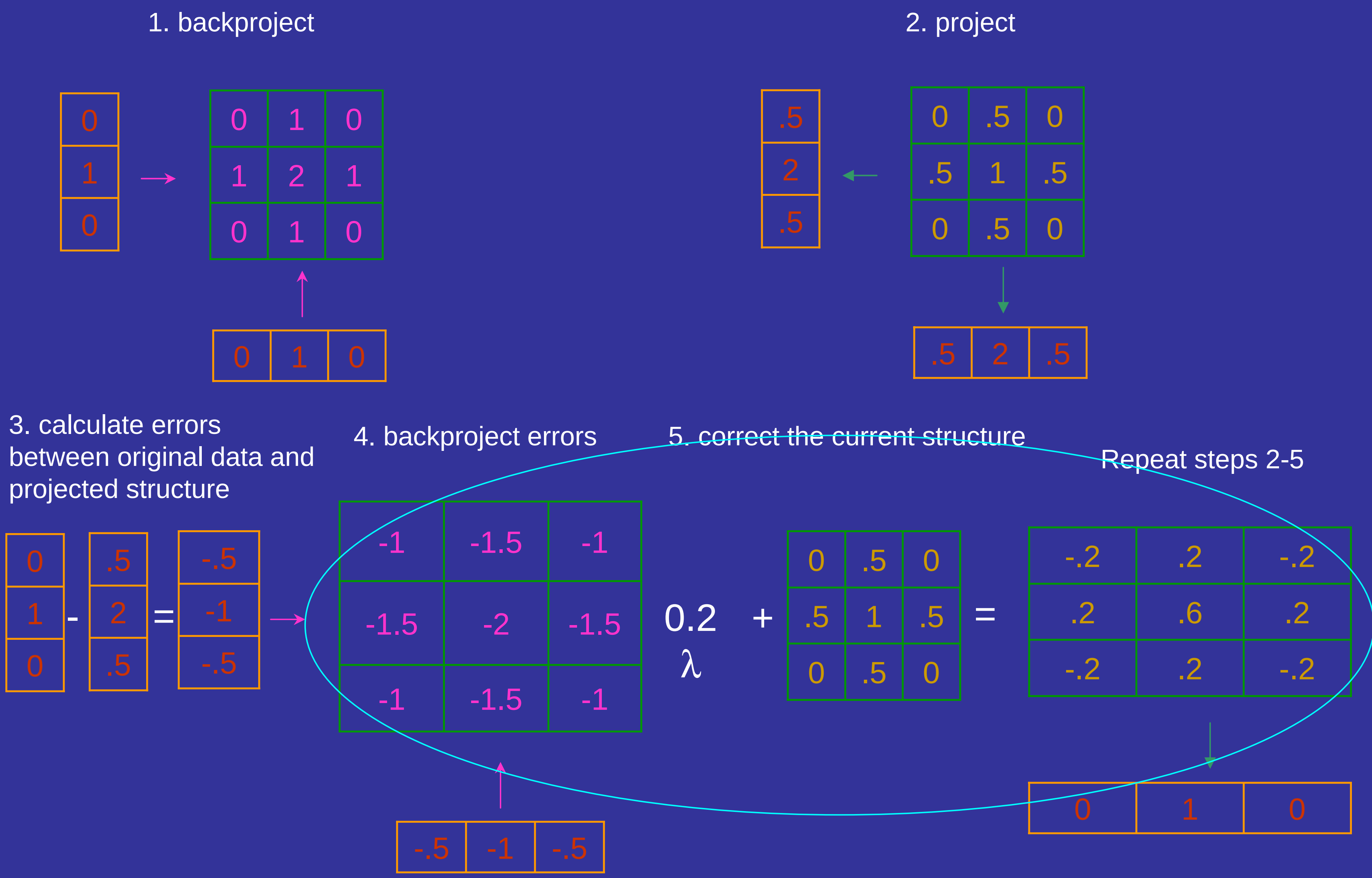
→

-2	0	-2
0	2	0
-2	0	-2

↑

-1	1	-1

Iterative improvement of the reconstruction



3D reconstruction algorithm can be considered the most important element of the single particle reconstruction process

Many steps of the process are best understood in terms of the 3D reconstruction problem:

- construction of an initial model
- refinement of the structure
- resolution estimation

The problem of 3D reconstruction from projections in EM is substantially different from the problem of "classical" tomography:

- data collection geometry cannot be controlled (random distribution of projection directions)
- extremely uneven distribution of projection directions, in many cases resulting in gaps in Fourier space
- extremely low SNR
- large errors in orientation parameters, both random and systematic, in principle the 3D reconstruction should be a part of orientation refinement procedure
- number of projection data much larger than the linear size of projections

Why the problem of 3D reconstruction from projections remains interesting?

- ✓ The problem is ill-posed – small change in the input data (2D projections) can cause large change in the results (3D structure).
- ✓ Unique solution does not exist!
- ✓ Various experimental situation may require different 3D reconstruction algorithms depending on the required accuracy of the results, amount of the input data, time constraints….

Ghosts do exist

(a theorem)

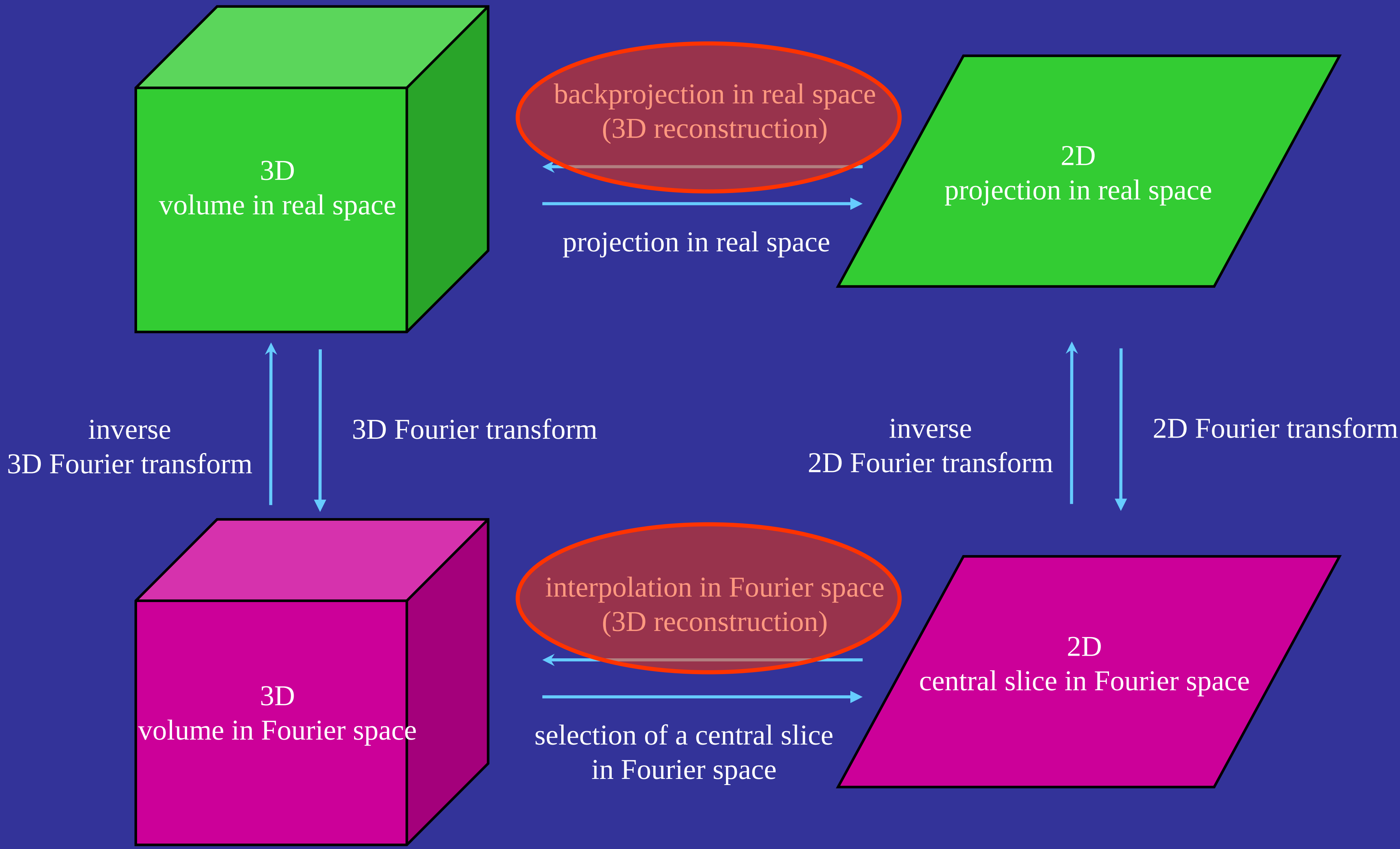
For any set of projection directions there exists a non-trivial object $f_0 \neq 0$ such that its projections at given directions are zero, that is $Pf_0 = 0$.

X=a+b	a -1	b+1
Y=c+d	c +1	d -1
	U=a+c	V=b+d

a ghost

-1	1
1	-1

Tomography (reconstruction from projections).



Difficult *inverse problems*, exact inversion does not exist!

Taxonomy of 3-D reconstruction methods

	Direct (solution obtained after one scan through the data)	Iterative (the structure is "improved" iteratively)
Algebraic	Direct solution of the system of equations defined by the projection matrix. Singular Value Decomposition (SVD) *Because of the size of the matrix not used in 3-D.*	1. Algebraic Reconstruction Technique (ART) 2. Simultaneous Iterative Reconstruction Technique (SIRT) *Very good results, very slow.*
Filtered backprojection (Fourier space filtration)	1. General Weighted Backprojection (Radermacher) 2. Exact Filter (Harauz & van Heel) Require construction of a weighting function in Fourier space – no exact formula exists. *Reasonably fast, reasonably accurate.*	Not used.
Direct Fourier inversion (Fourier space interpolation)	Gridding algorithm (Penczek) Requires full coverage of Fourier space by projection data. *The most accurate method, fast.*	Not used.

Algebraic methods

Find vector $\tilde{f}$ that minimizes $L(f) = \|Pf - g\|^2$.

Find a 3-D structure such that 2-D projections are most similar (in the Least Squares sense) to given 2-D data.

Algorithms:

ART – Algebraic Reconstruction Technique.
Kaczmarz's row action iterative algorithm for solving a system of linear equations.

SIRT – Simultaneous Iterative Reconstruction Technique:
(1) chose initial 3-D structure $f^{(0)}$ (usually zero);
(2) modify 3-D structure by a gradient $\nabla L(f)$
(3) repeat step 2 until convergence is reached.

Important features:

For the SIRT algorithm, the solution does not depend on the starting point.

Rate of convergence: SIRT - 100; ART - 10.

Twiddle knobs – number of iterations and λ.

If incorrectly selected, will either cause premature termination and incorrect result or, if number of iterations or λ too small, will result in a structure lacking high-frequency details.

The parameters have to be adjusted for each data set separately.

If iterative algorithms are slow and inconvenient, why would we want to use them?

- The quality of results surpasses the quality of results of other methods, particularly of those based on Fourier transform. Least disturbing artifacts.

- SIRT algorithms perform better in "extreme" situations, such as uneven distribution of projections, incomplete projections ("missing cone", "missing wedge"), reconstruction from few directions.

- SIRT algorithms are flexible. It is possible to incorporate additional constraints (positivity, limited spatial support), *a priori* knowledge, CTF correction….

Filtered Back-Projection algorithm

1. for each 2-D projection construct a 2-D weighting filter taking into account distribution of remaining projections (*slow and inaccurate*)

2. filter each 2-D projection using respective 2-D filter

3. back-project filtered 2D projections (in real space, *fast and easy*)

Twiddle knobs:
Usually hidden from the user. For a given parameter value, algorithms perform equally well in a broad range of situations.

Direct Fourier inversion

1. calculate 2-D Fourier transform of a projection and using an interpolation scheme place it within a 3-D (Fourier) volume with additional weighting to account for uneven distribution of projections (*very difficult if done properly*)

2. calculate inverse 3D Fourier transform (*fast and easy*)

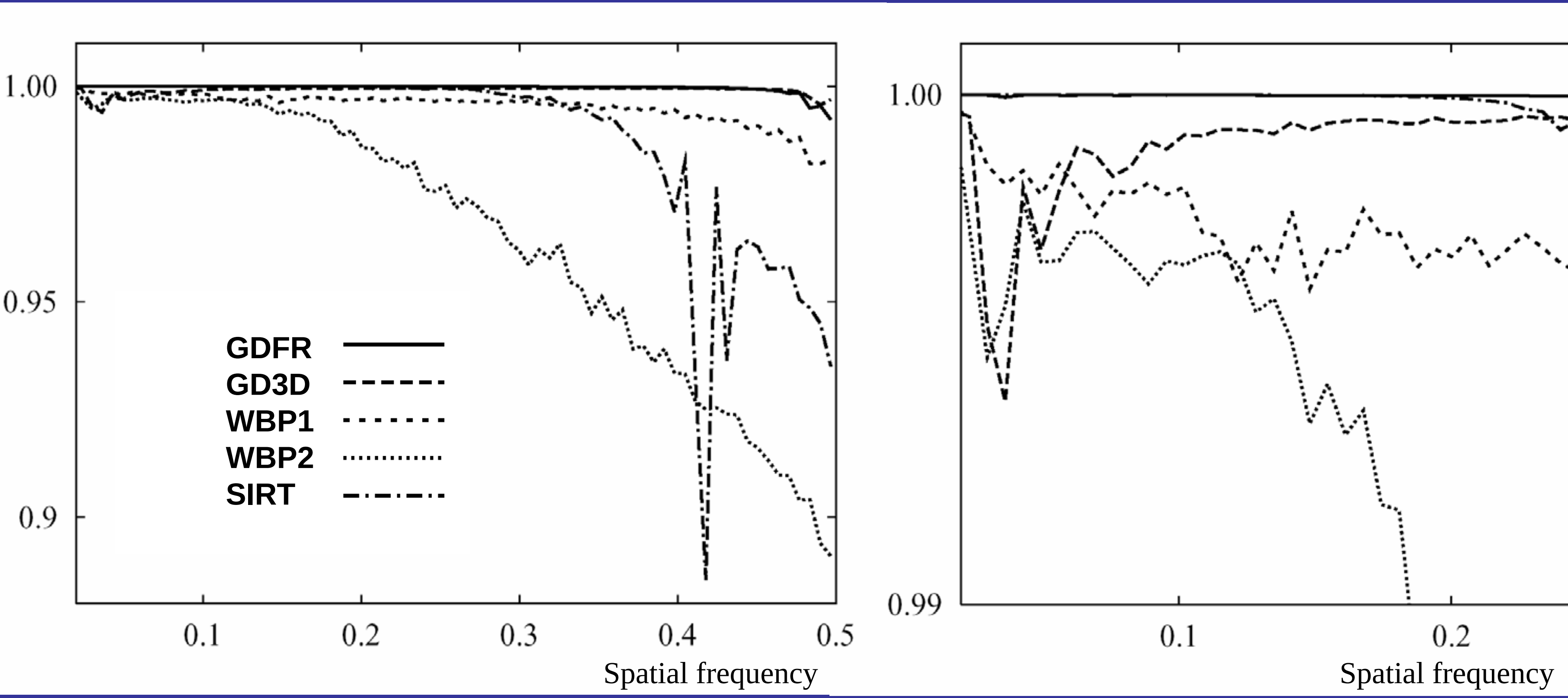
Twiddle knobs:
Usually hidden from the user. For a given parameter value, algorithms perform equally well in a broad range of situations.

Fidelity curves

FSC between the test object and computed structure

no noise, projection data by reverse gridding

Gridding algorithm, Voronoi weights	GDFR	0.98584
Gridding algorithms, approximate weights	GD3D	0.98436
General weighting filtered bp	WBP1	0.97927
Exact weighting Filtered bp	WBP2	0.97228
SIRT	SIRT	0.98055



Summary

- Cryo-EM and single particle reconstruction rely on the tomographic effect in the electron microscope.

- There is no unique solution to the problem of recovering the 3D structure from the finite set of its 2D projections.

- The quality and speed of 3D reconstruction algorithms differ. Generally, the speed and quality are inversely proportional. Depending on the data set (presence end level of noise, errors, gaps in angular coverage) some algorithms perform better than other.

SIRT: (Gilbert, 1972; Penczek *et al.*, 1992; Penczek *et al.*, 1997; Zhu *et al.*, 1997)

ART: (Gordon *et al.*, 1970; Marabini *et al.*, 1998)

General Weighting Back-Projection: (Radermacher, 1992; Radermacher *et al.*, 1986)

Exact Weighting Back-Projection: (Harauz and van Heel, 1986)

Direct Fourier inversion: (Penczek *et al.*, 2004)

1. Gilbert, H., 1972. Iterative methods for the three-dimensional reconstruction of an object from projections. Journal of Theoretical Biology 36, 105-117.
2. Gordon, R., Bender, R., Herman, G. T., 1970. Algebraic reconstruction techniques (ART) for three-dimensional electron microscopy and x-ray photography. Journal of Theoretical Biology 29, 471-81.
3. Harauz, G., van Heel, M., 1986. Exact filters for general geometry three dimensional reconstruction. Optik 73, 146-156.
4. Marabini, R., Herman, G. T., Carazo, J. M., 1998. 3D reconstruction in electron microscopy using ART with smooth spherically symmetric volume elements (blobs). Ultramicroscopy 72, 53-65.
5. Penczek, P., Radermacher, M., Frank, J., 1992. Three-dimensional reconstruction of single particles embedded in ice. Ultramicroscopy 40, 33-53.
6. Penczek, P. A., Renka, R., Schomberg, H., 2004. Gridding-based direct Fourier inversion of the three-dimensional ray transform. J. Opt. Soc. Am. A 21, 499-509.
7. Penczek, P. A., Zhu, J., Schröder, R., Frank, J., 1997. Three-dimensional reconstruction with contrast transfer function compensation from defocus series. Scanning Microscopy Supplement 11, 1-10.
8. Radermacher, M. (1992) Weighted back-projection methods, *in* J. Frank (Ed.), Electron Tomography, pp. 91-115, Plenum, New York.
9. Radermacher, M., Wagenknecht, T., Verschoor, A., Frank, J., 1986. A new 3-D reconstruction scheme applied to the 50S ribosomal subunit of *E. coli*. Journal of Microscopy 141, RP1-RP2.
10. Zhu, J., Penczek, P. A., Schröder, R., Frank, J., 1997. Three-dimensional reconstruction with contrast transfer function correction from energy-filtered cryoelectron micrographs: procedure and application to the 70S *Escherichia coli* ribosome. J. Struct. Biol 118, 197-219.