Generalized Ray Transforms in Electron Microscope Tomography

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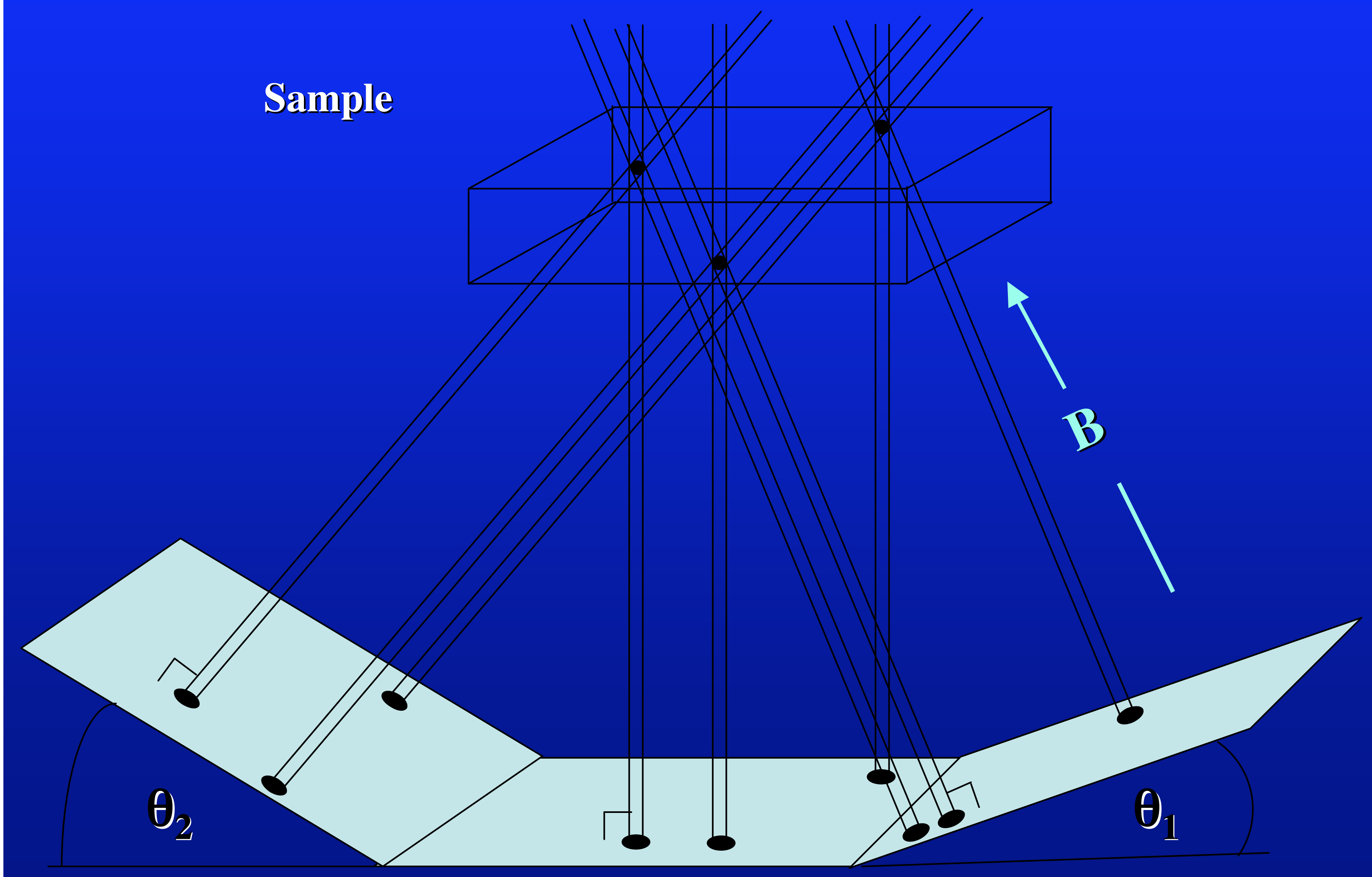
Application of Generalized Ray Transforms in Large-Field Electron Microscope Tomography

- Introduction
  - What is EM Tomography?
  - Why do EM Tomography?
  - How does EM Tomography differ from conventional X-ray tomography?
- Mathematical model
- Present code (TxBR)
- Three problems
  - Alignment
  - Rebinning
  - Filtering

What Is EM Tomography?

Standard Tomography
Single Axis



Why Do EM Tomography

- Eliminate shadowing
- Elucidate 3D Structure

Elimination of Shadowing Effects via Electron Microscope Tomography

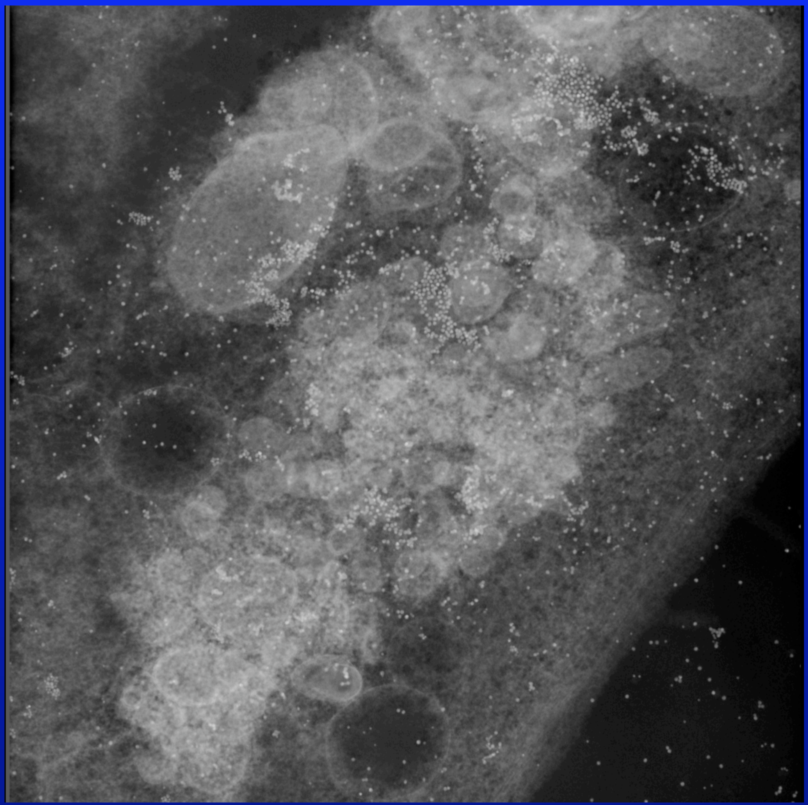
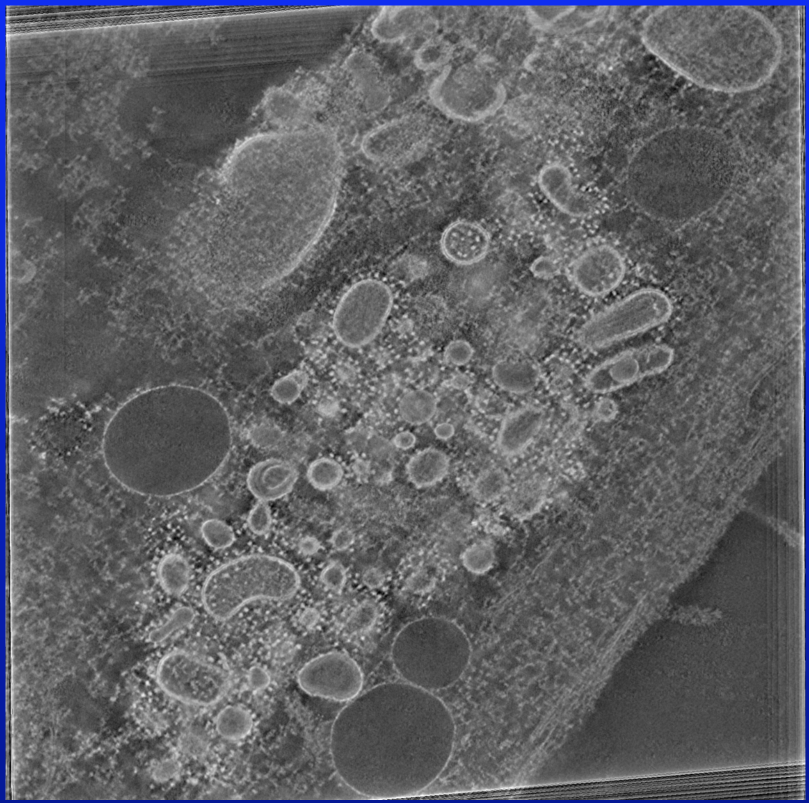


Image data, no rotation

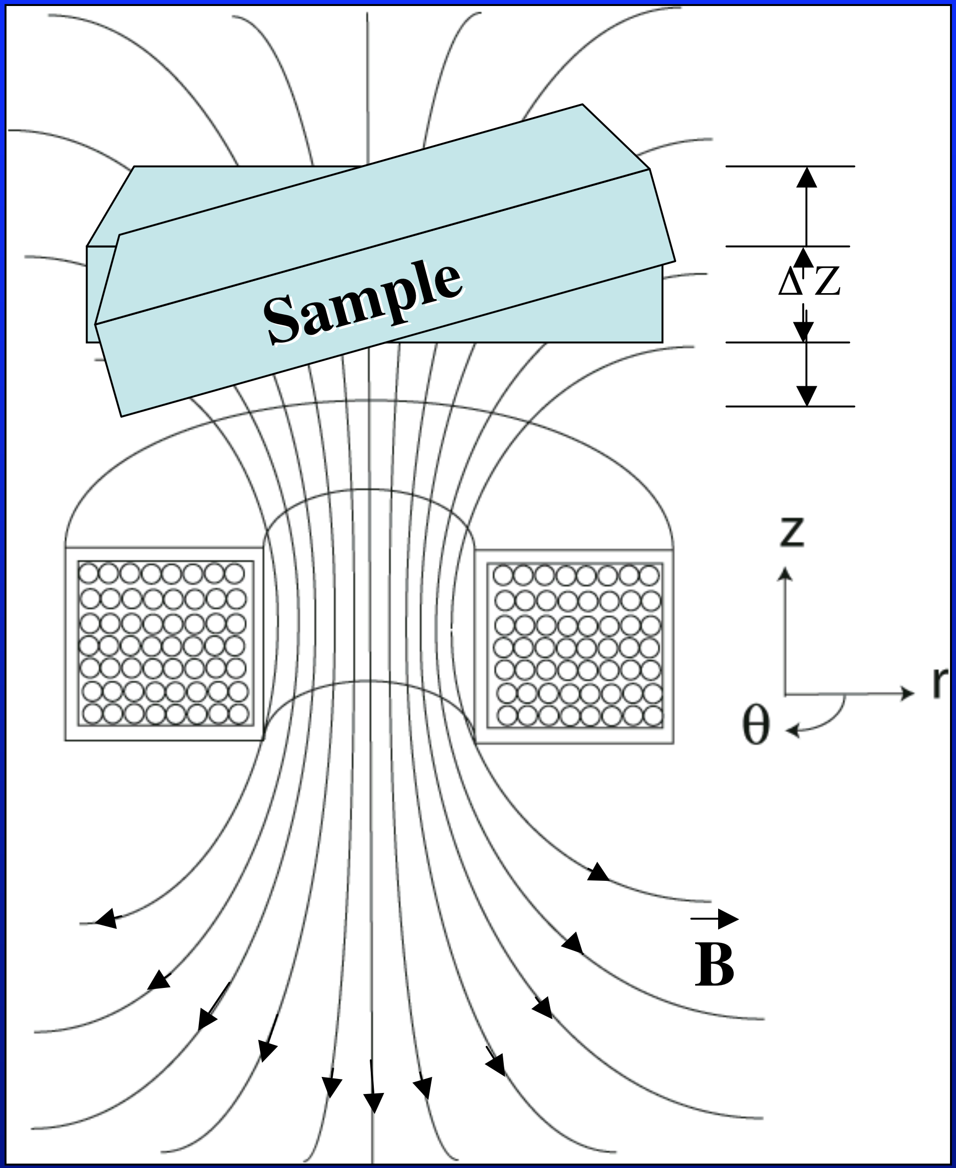


Section of 3D reconstruction

Technical Problems in EM Tomography

- Noise. Imaging is through electrons scattering out from beam.
- Limited data. Exponential decrease of flux thru sample at high angles.
- Positioning accuracy. Sub micron information required.
- Magnetic lenses. Electrons travel in helical paths in focusing fields.
- High energy electrons, Structure degradation. Number of angles exposure-limited.
- Sample mass loss. Sample warping.
- Imperfect lenses. Aberrations. Image distortion.

Fringing Fields Affect Image Formation

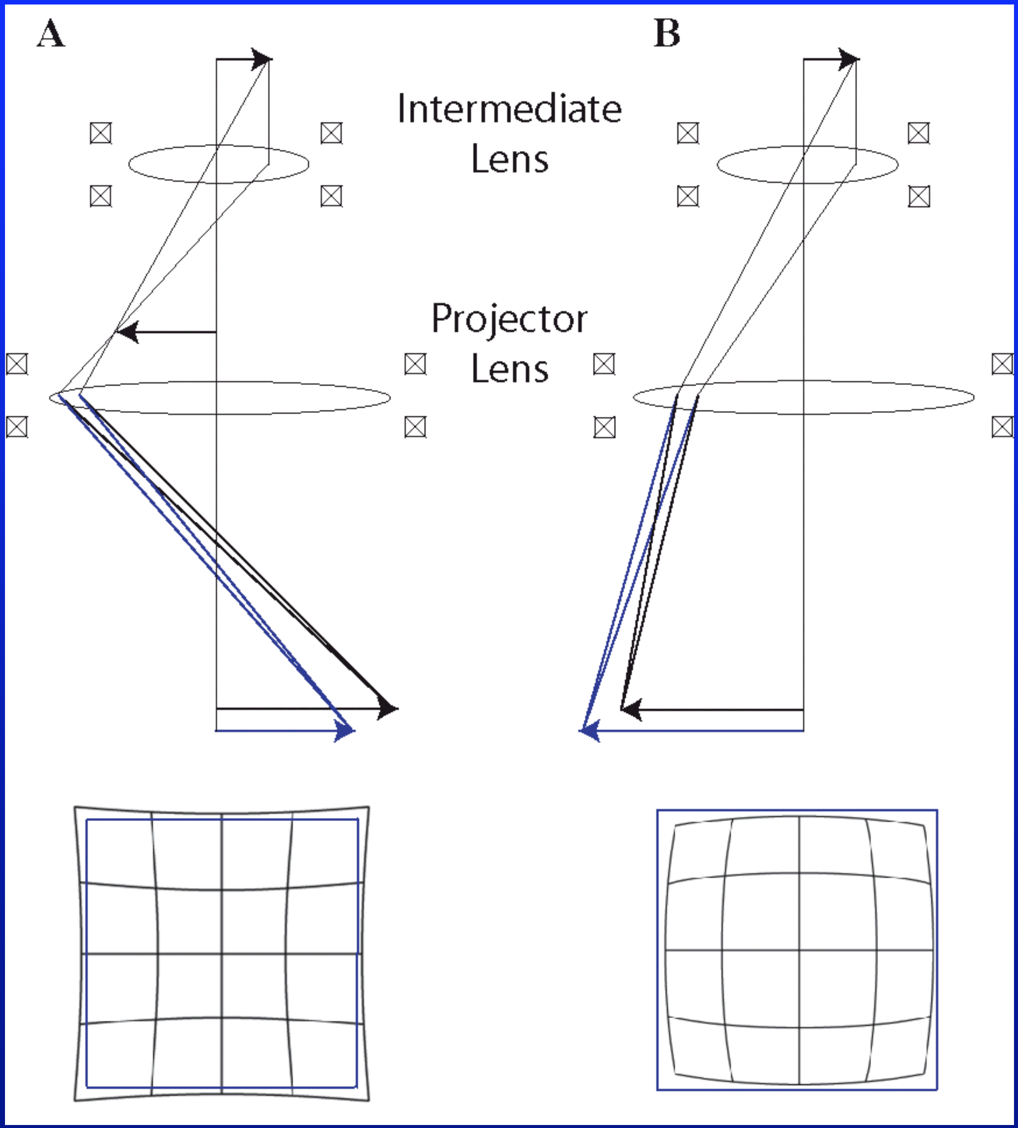


- Differential magnification
- Differential rotation
- More pronounced for large format images
- Rotation and magnification are troublesome for tomography

$$\theta_L \propto B_z(r,z)$$ (rotation)

$$\frac{\Delta M_{ag}}{M_{ag}} = \frac{\Delta z}{f}$$ (magnification)

Spherical Aberration Produces Spatial Distortion

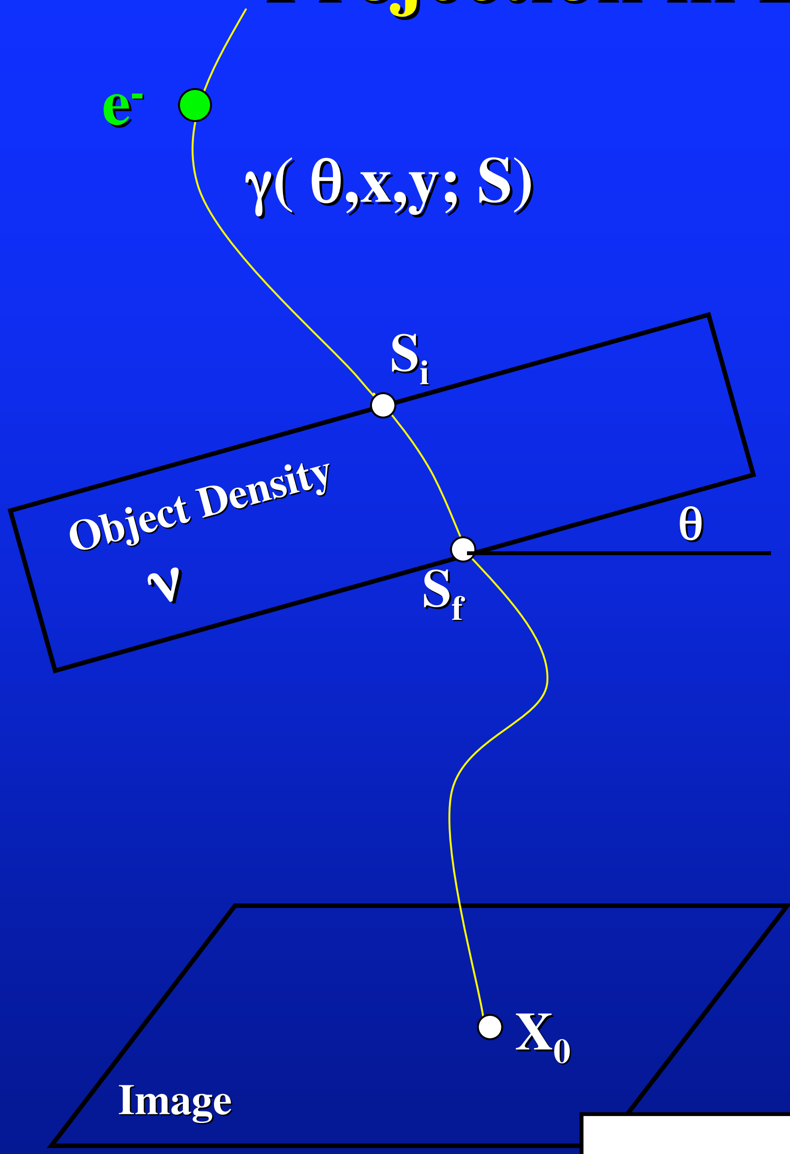


Spherical aberration results from a change in focus in center vs outer edge of lens

Virtual image produces barrel distortion

Real image at projection produces pincushion distortion

Projection in Electron Microscope



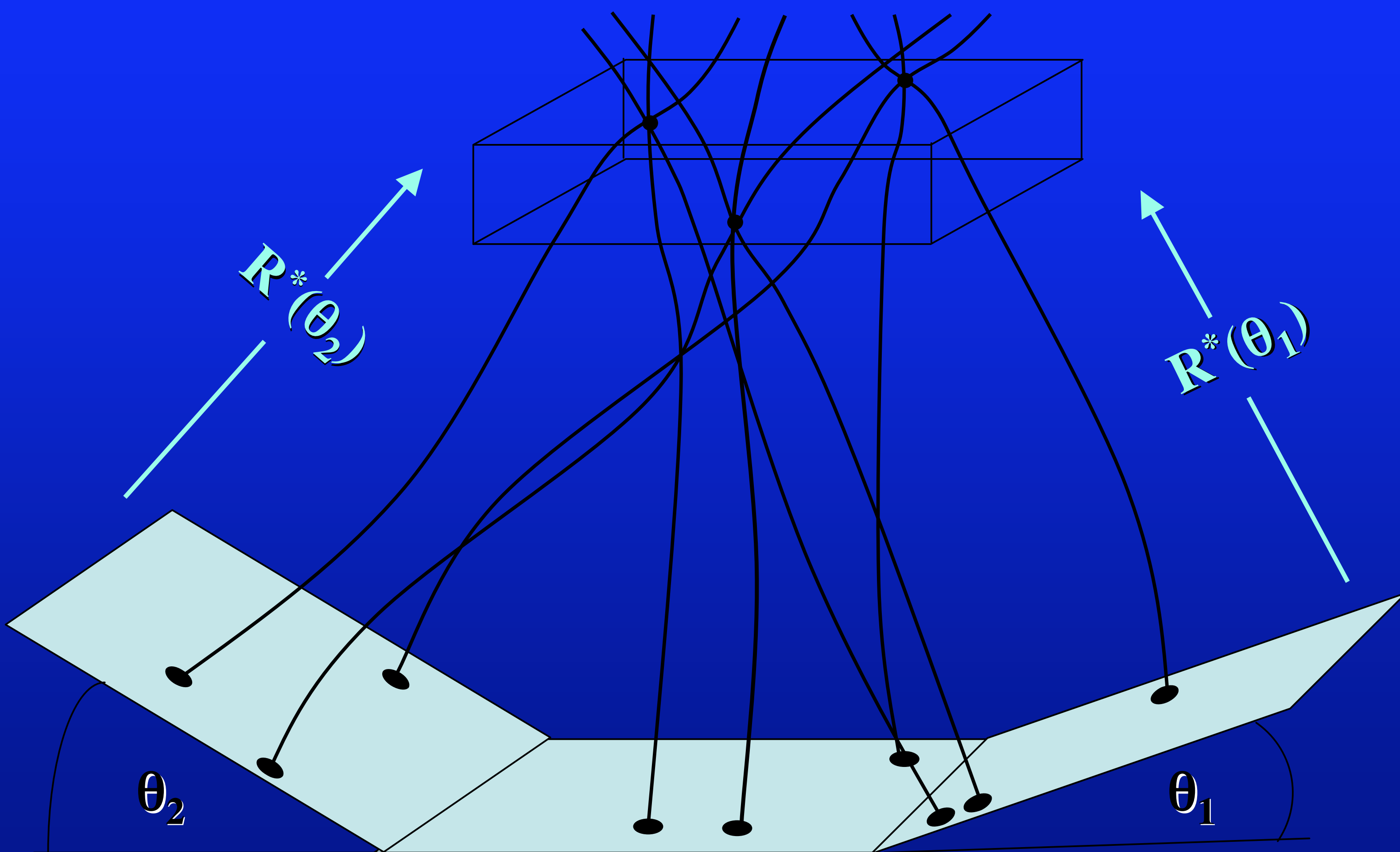
- γ = electron path
- S_i = point of entrance
- S_f = point of exit
- θ = tilt angle
- $X_0 = (x, y)_{image}$
- $X = (x,y,z)$
- ν = object density fxn
- $\hat{u}$ = image intensity

Linear "single scattering model"

$$\hat{u}(\theta,x,y) = u_0 \cdot e^{-\int_{S_i}^{S_f} \nu(\gamma(\theta,x,y;s))ds}$$

$$u = \ln(\hat{u}(\theta,x,y)) - \ln(u_0) = -\int_{S_i}^{S_f} \nu(\gamma(\theta,x,y;s))ds$$

Projection Along Curvilinear Trajcetories



Mathematical Model

$$\Gamma = \{\gamma_{(\theta;x,y)}\}$$

Family of trajectories Indexed by image point and sample angle.

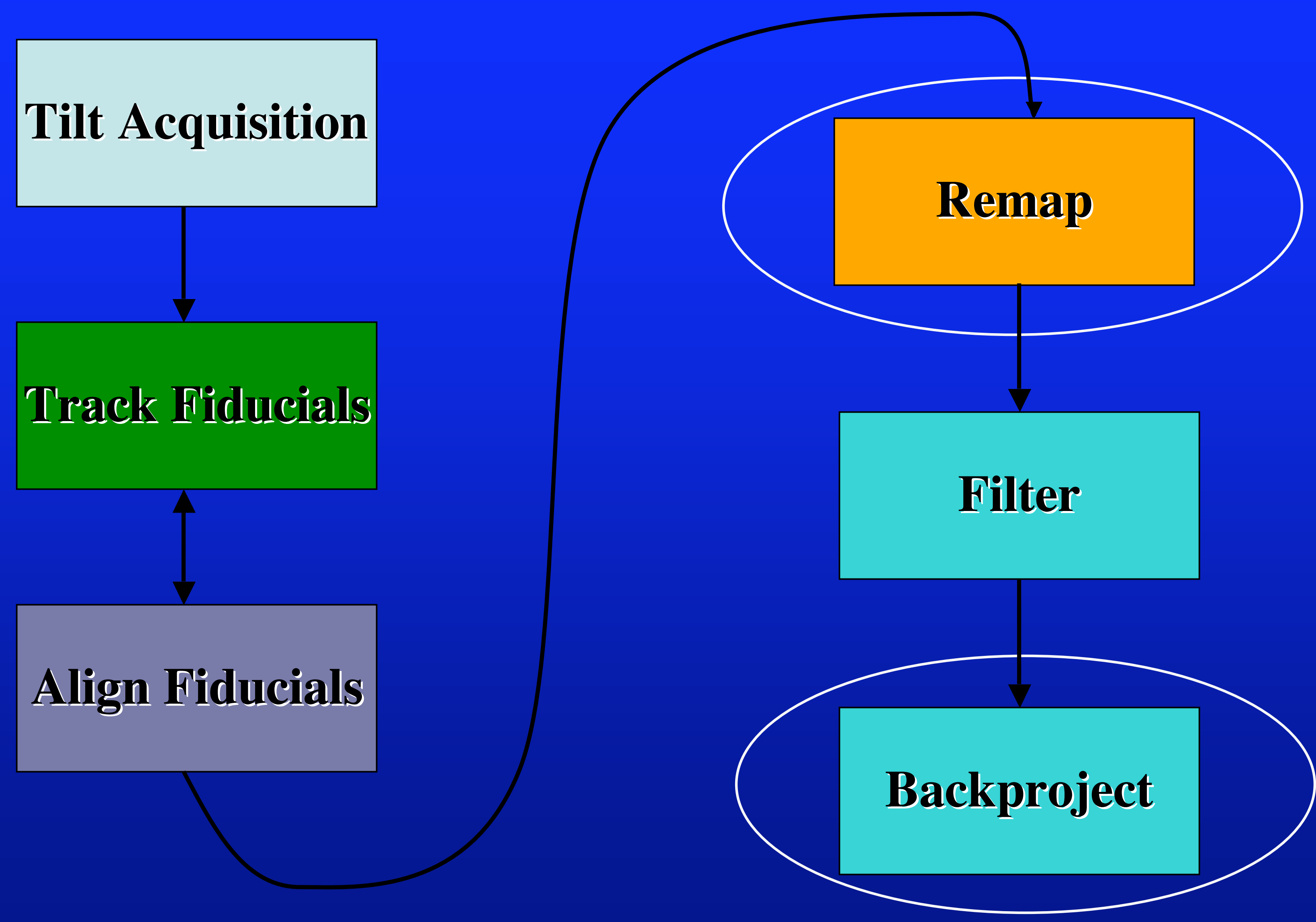
$$R_\Gamma u(\theta;x,y) = \int_{s=s_i}^{s=s_f} u(\gamma_{(\theta;x,y)}(s))ds$$

Transform defined by integration of density along trajectories

$$R_\Gamma^* v(x,y,z) = \int_{\gamma_{(\theta;x,y)}(s)=(x,y,z)} R_\Gamma u(\theta;x,y)d\theta$$

Adjoint transform defined by integration over sample orientations

Tomography Workflow

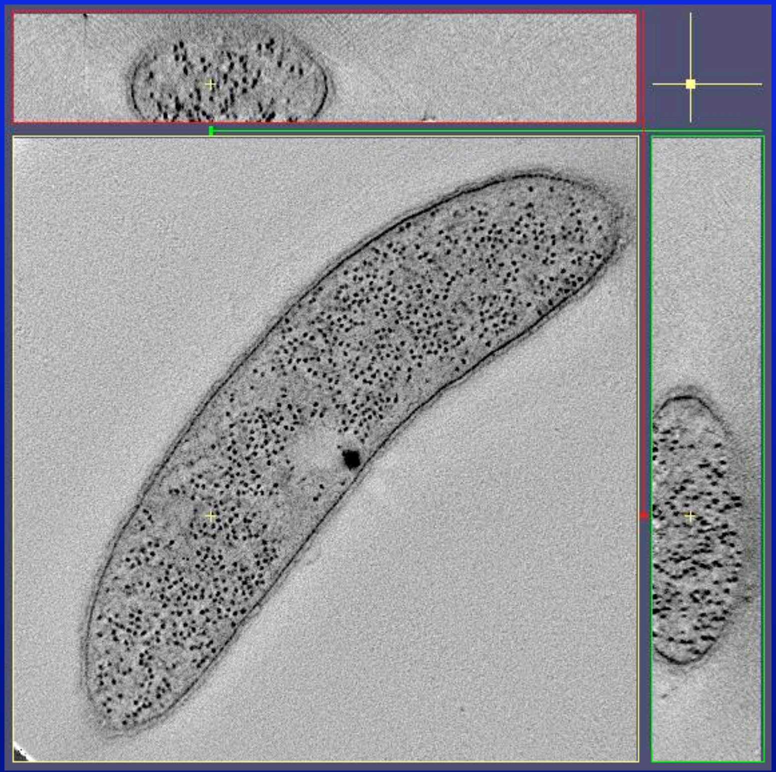


Reconstruction

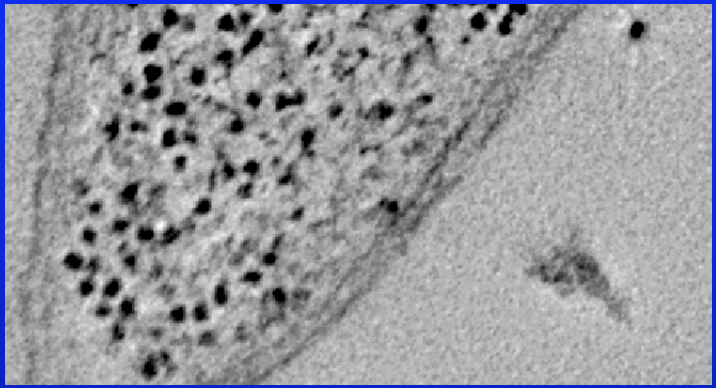
- Present code (TxBR): filtered backprojection
  - Alignment on point-like markers
  - Multiple tilt axes
  - Iterated bundle adjustment; initial estimate via projective duality
  - Best orthogonal model for markers and projection maps
  - Corrections up to 6th order
  - Rebinning via image warping
  - 1D filtration along best straight line fitting of feature tracks
  - Backprojection along implicit electron trajectories
  - Fast calculation of forward maps via Nth order differences

TxBR Reconstruction for Curvilinear Electron Paths

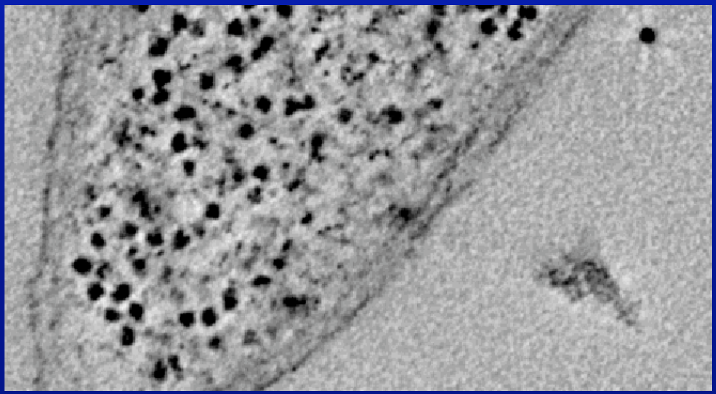
3D TxBR Reconstruction of a Caulobacter Crescentus from 2kx2k electron micrograph



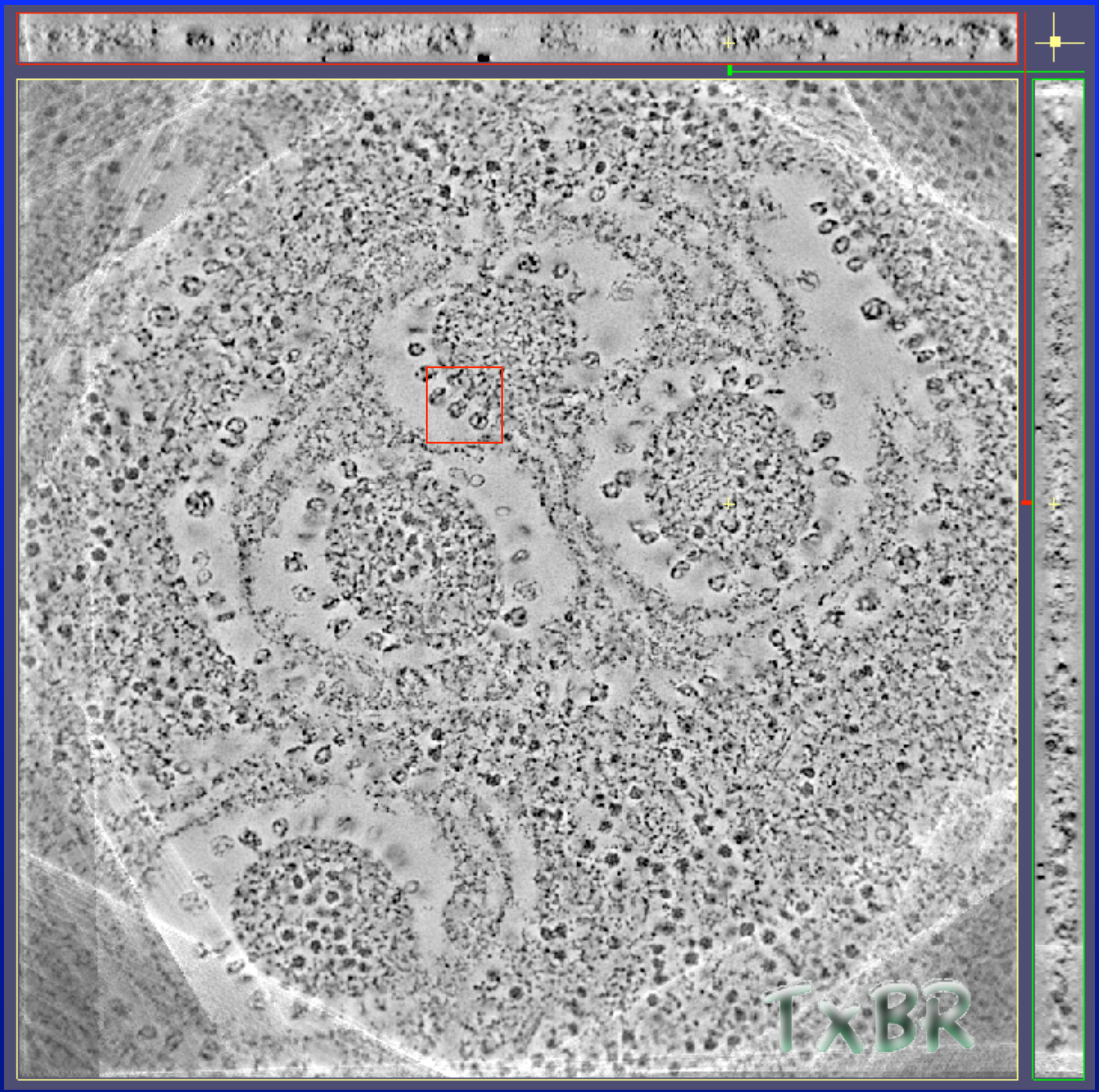
order 1: Reproj. Err.~0.95px

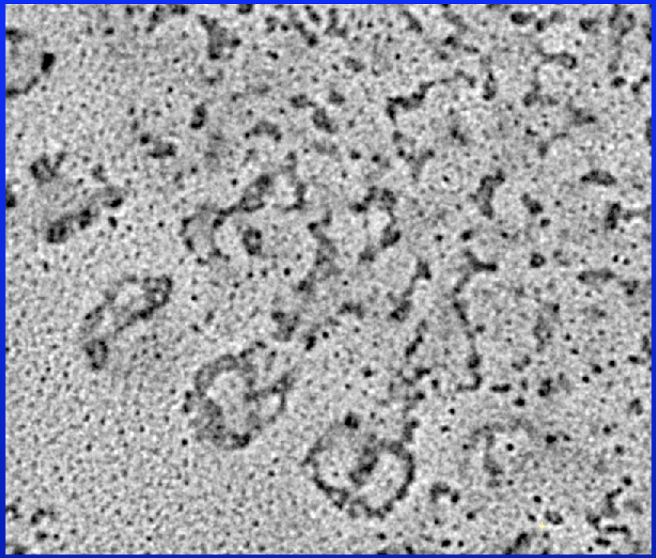


order 3: Reproj. Err.~0.3px



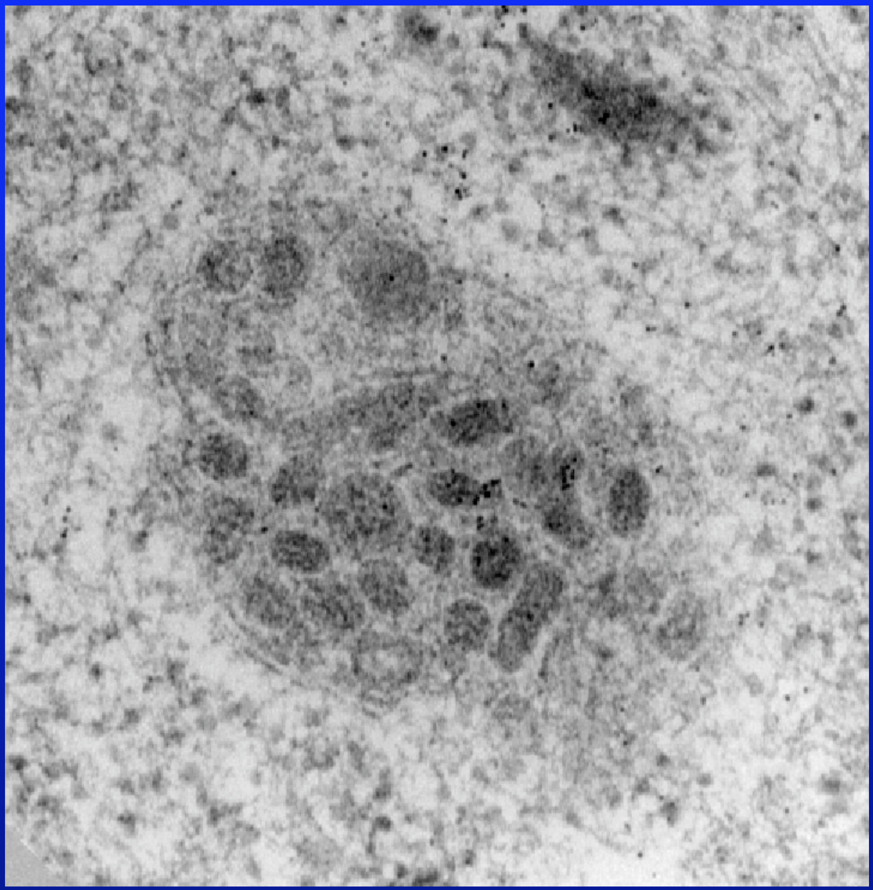
TxBR Reconstruction on a 8kx8k dataset

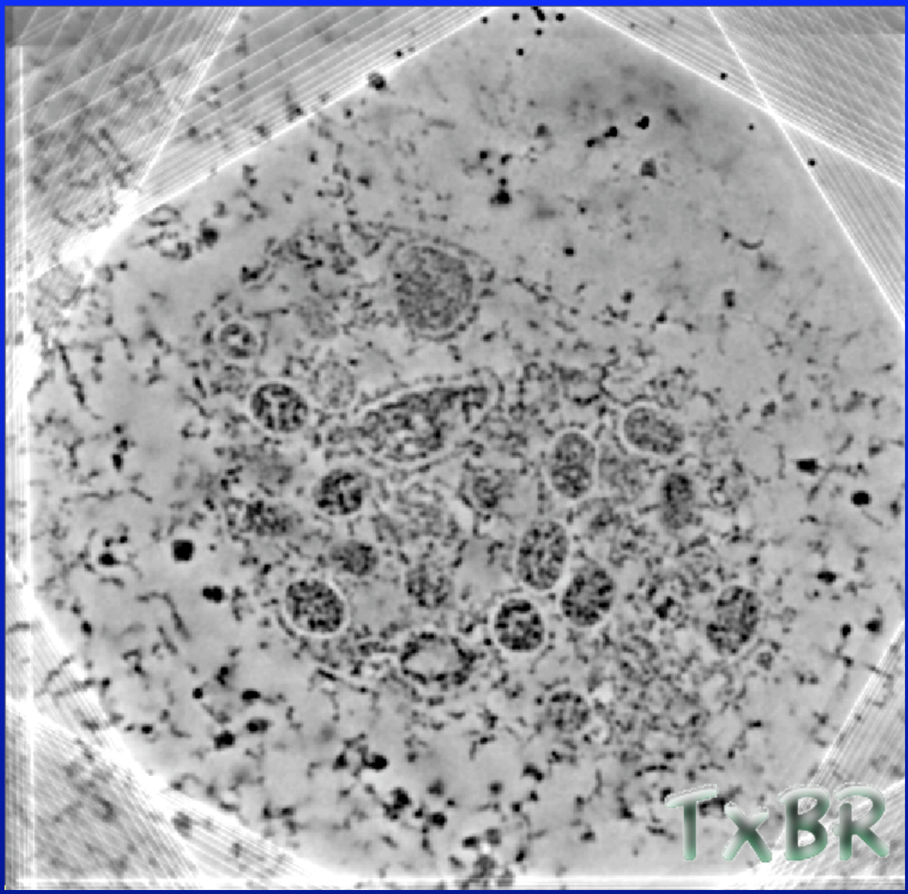




Flock House Viruses Study

Reconstruction of a sextuple tilt series





Influenza Virus

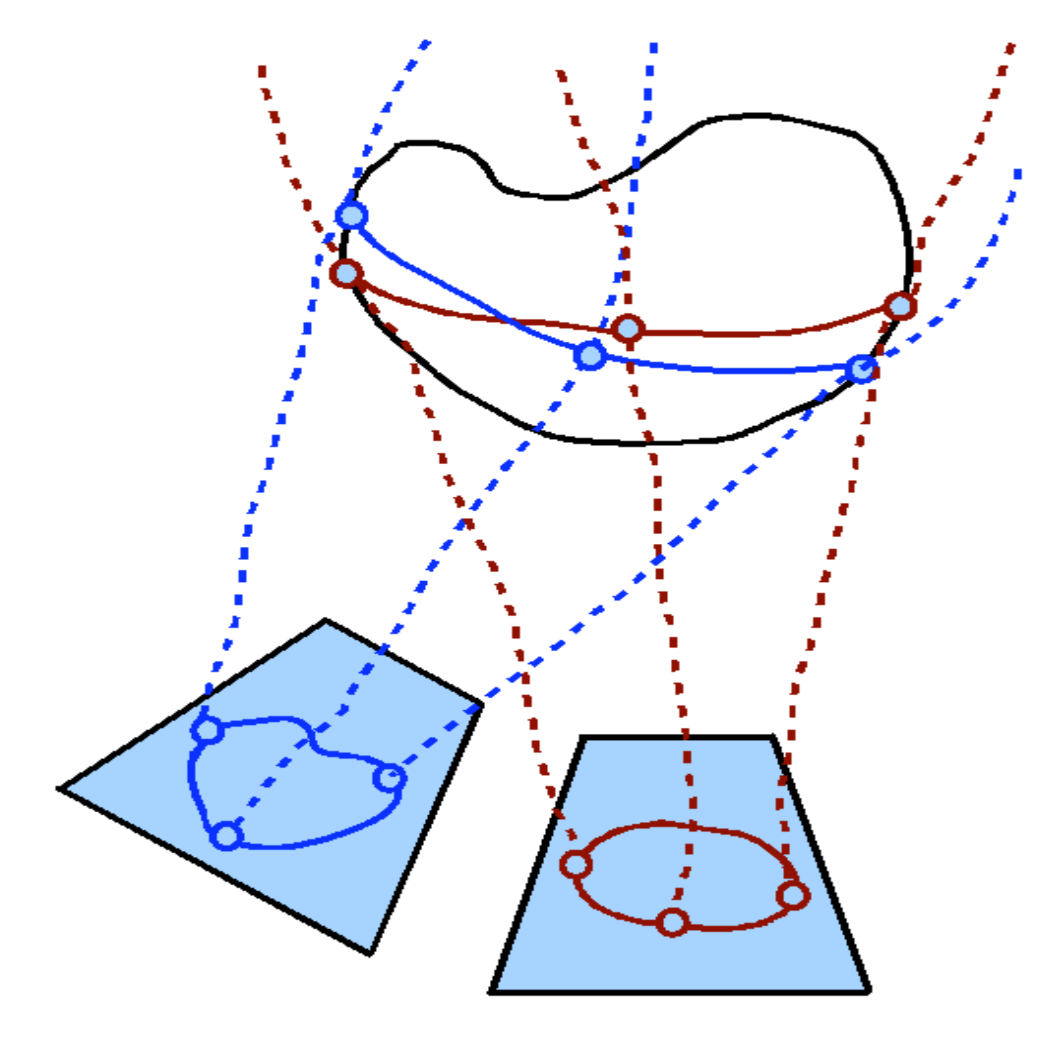
Extensions to the Code

- Alignment on spatially extended image features. Use contours which are projections of surface along rays.
- 3D rebinning of image pixels. Calculate integral along trajectories not in data set without prior reconstruction.
- Exact filters for general curvilinear trajectories. and more general sets of image orientations. Filter after backprojection via spatially dependent kernels.

Contour Alignment

- Biological samples contain extensive membrane structures
- Staining generally occurs along surfaces
- Surfaces project to contours in images
- Rays projecting to contours are tangent to surfaces along paths on surface
- Projective duality generalizes to projection along curvilinear trajectories
- Method of occluding contours gives initial estimate of projection maps and surfaces

Projection Along Rays



- Curvilinear rays tangent to surface
- Contour in surface projects to contour in image
- Geometric objects parameterized by polynomial expressions

Contour Alignment Model and Error Terms

$$\left(x_{1\omega k}^{(p)}, x_{2\omega k}^{(p)}\right) = P \circ S\left(r_{1\omega}(\rho_{\omega k}), r_{2\omega}(\rho_{\omega k})\right)$$

$$\left(X_{1\omega k}^{(p)}, X_{2\omega k}^{(p)}, X_{3\omega k}^{(p)}\right) = S\left(r_{1\omega}(\rho_{\omega k}), r_{2\omega}(\rho_{\omega k})\right)$$

$$\left(X_{1\omega k}^{(d)}, X_{2\omega k}^{(d)}, X_{3\omega k}^{(p)}\right) = \gamma_{\left(\omega; x_{1\omega k}^{(d)}, x_{1\omega k}^{(d)}\right)}\left(X_{3\omega k}^{(p)}\right)$$

$$E_1 = \sum_{\omega k} \left\| \left(x_{1\omega k}^{(p)}, x_{2\omega k}^{(p)}\right) - \left(x_{1\omega k}^{(d)}, x_{2\omega k}^{(d)}\right) \right\|^2$$

$$E_2 = \sum_{\omega k} \left\| \left(X_{1\omega k}^{(p)}, X_{2\omega k}^{(p)}, X_{3\omega k}^{(p)}\right) - \left(X_{1\omega k}^{(d)}, X_{2\omega k}^{(d)}, X_{3\omega k}^{(p)}\right) \right\|^2$$

$$E_3 = \sum_{\omega k} \left(\gamma_{\left(\omega; x_{1\omega k}^{(d)}, x_{1\omega k}^{(d)}\right)} \cdot \left(\frac{\partial S\left(r_{1\omega}(\rho_{\omega k}), r_{2\omega}(\rho_{\omega k})\right)}{\partial r_1} \times \frac{\partial S\left(r_{1\omega}(\rho_{\omega k}), r_{2\omega}(\rho_{\omega k})\right)}{\partial r_2} \right) \right)$$

- **Points along contours in surface patch imbed in 3D object and project to contours in image**
- **Data points in image backproject to points in slice specified by third coordinate**
- **Error terms compare projected points, back projected points and specify orthogonality conditions**

Consistency Equations and Rebinning

$$Rf(\xi,\eta) = \int_0^1 f(s\xi + (1-s)\eta)\,ds$$

$$\frac{\partial^2 Rf}{\partial\eta_i \partial\xi_j} = \frac{\partial^2 Rf}{\partial\eta_j \partial\xi_i}$$

- **Affine version of X-ray transform**
- **Consistency conditions: John equations**

$$\gamma_{(a,b)}(s) = (a_0 + a_1 s + \ldots + a_n s^n, b_0 + b_1 s + \ldots + b_n s^n, s)$$

$$R_\Gamma f = \int_{S_i}^{S_f} f\left(\gamma_{(a,b)}(s)\right) ds$$

$$\frac{\partial^2 R_\Gamma f}{\partial a_i \partial b_j} = \frac{\partial^2 R_\Gamma f}{\partial a_j \partial b_i}$$

- **Electron trajectories approximated by polynomials**
- **Generalized ray transform**
- **Consistency comditions**

Application of the Fritz John Equations

- Equations constitute boundary value problem
- Transform along known trajectories from experimental data
- Solve equations to obtain transform along unknown trajectories
- Calculate matching trajectories in overlap regions for montaging
- Construction of synthetic tilts for artifact control

Setting Up the Transform as a Fourier Integral Operator

$$\Omega_\theta : (X,Y,Z) \rightarrow \gamma_{\theta;X,Y}(Z)$$

$$\Pi_\theta{}^{aug}(X,Y,Z) = (\Pi_\theta(X,Y),Z)$$

$$\Omega_\theta \Pi_\theta{}^{aug} = I$$

$$A_\theta(X,Y,Z) = R_\theta{}^{-1}(\Omega_0(R_\theta(X,Y,Z)))$$

$$\overline{R_\Gamma u}(\omega) = I_\Gamma \bar{u}(\omega) =$$

$$\frac{1}{(2\pi)^3} \iint e^{i(x \cdot \xi - \omega \cdot A_\theta^{-1}(x))} \det(A_\theta^{-1}(x)) \bar{u}(\xi)\, dx\, d\xi$$

Electron trajectories define coordinate transform

Inverse transforms

Constant beam model

FIO as coordinate transform

Coordinate Changes

$$
\begin{tikzcd}
C_0(\mathbb{R}^3) \arrow[d, "R_\theta^{-1*}"] & C_0(\mathbb{R}^3) \arrow[l, "\Omega_0^*"'] \arrow[d, "R_\theta^{-1*}"] & C_0(\mathbb{R}^3) \arrow[l, "\Pi_0^*"'] \arrow[ll, bend right, "Id"'] \\
C_0(\mathbb{R}^3) & C_0(\mathbb{R}^3) \arrow[l, "(Ad(R_\theta^{-1})\Omega_0)^*"]
\end{tikzcd}
$$

Apply formula for coordinate change and Fourier Slice theorem.

Operator Theory for Filters

$$u + Tu = R_\Gamma^* F R_\Gamma u = R_\Gamma^* F v$$

$$\Psi = R_\Gamma^* R_\Gamma$$

$$u = \Psi^{-1} R_\Gamma^* v$$

- **In general, filtered backprojection works only up to an error term. For some special cases *T* → *0.***

- **A theorem of Gelfand states that the composition of a ray transform with its adjoint is an elliptic pseudo-differential operator.**

- **Heuristically, we would like to invert the operator, and compose with the adjoint ray transform.**

End Note

- Transform-based backprojection for volume reconstruction of large format electron microscope tilt series, A. Lawrence, J. C. Bouwer, G. Perkins and M. H. Ellisman, Journal of Structural Biology, 154:144-167 (2006).
- Tomography of Large Format Electron Microscope Tilt Series: Image Alignment and Volume Reconstruction, CISP-08, Sanya, China, May 2008,

- Reprints available.

Thank You for Your Attention