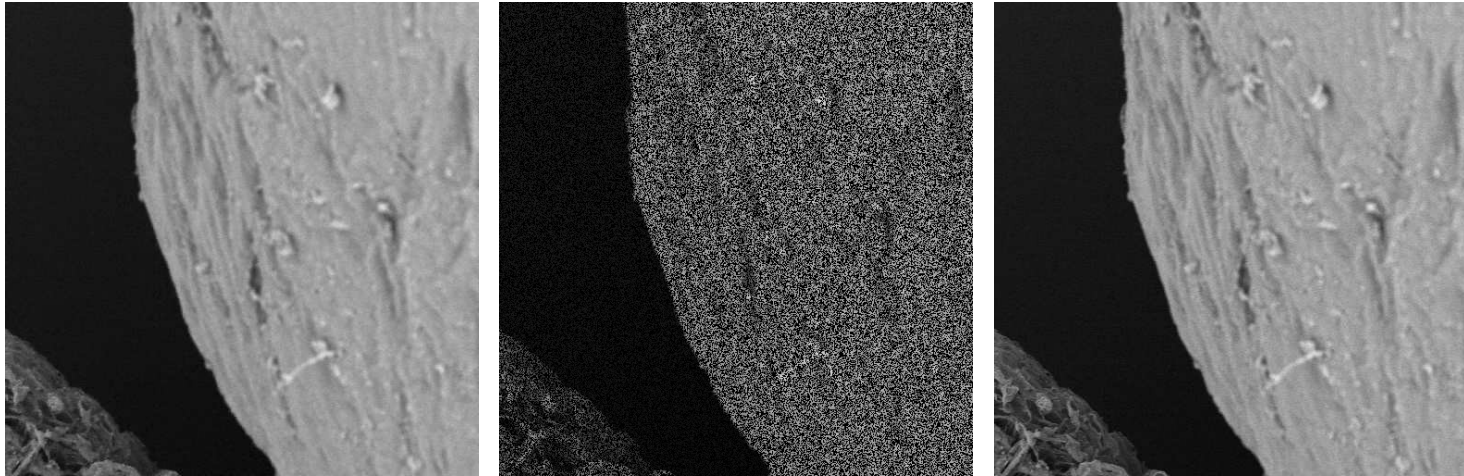


Exceptional service in the national interest



Compressed Sensing for fast electron microscopy

Hyrum Anderson, Jason Wheeler, Kurt Larson

Sandia National Laboratories

Albuquerque, NM



Sandia National Laboratories is a multi-program laboratory managed and operated by Sandia Corporation, a wholly owned subsidiary of Lockheed Martin Corporation, for the U.S. Department of Energy's National Nuclear Security Administration under contract DE-AC04-94AL85000. SAND NO. 2011-XXXXP

Outline

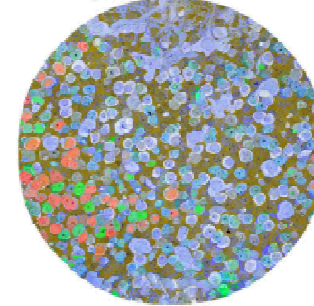
- Background and Motivation
- Previous work: sparse sampling an operational SEM
- Analysis of multi-beam measurements
- Summary

SNR-limited image collection time

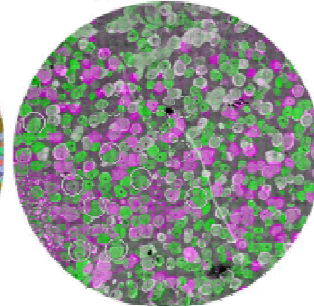
- Rabbit retina connectome (Anderson, et al., 2011)

- Tissue ~ 0.25 mm in diameter
- ~2 nm resolution
- 350,000 image tiles (16.5 TB) in 5 months
- Automated trans. electron microscope

A 001 $\gamma_{GE, \tau Q} = RGB_{\alpha}$



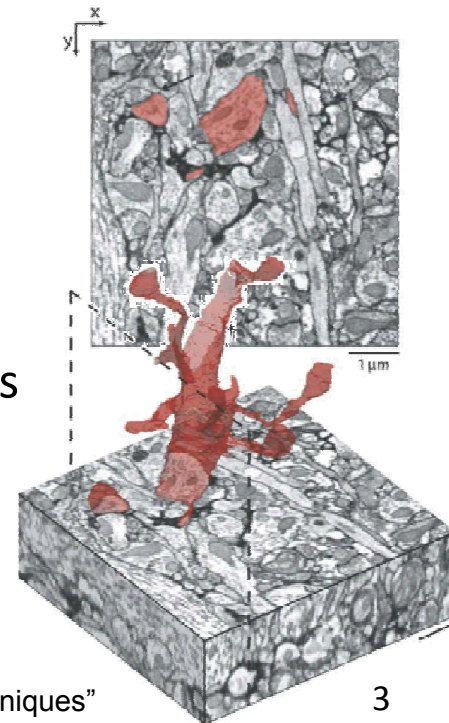
B 030 $\gamma_G = MG$



Anderson, et al., 2011, "Exploring the retinal connectome"

- Mouse brain (Briggman and Denk, 2006)

- Single cortical column from mouse ~0.1 mm³
- ~10nm / pixel per 30nm slice
- Thousands of images (10⁸ pixels each) over several months
- Serial block-face SEM

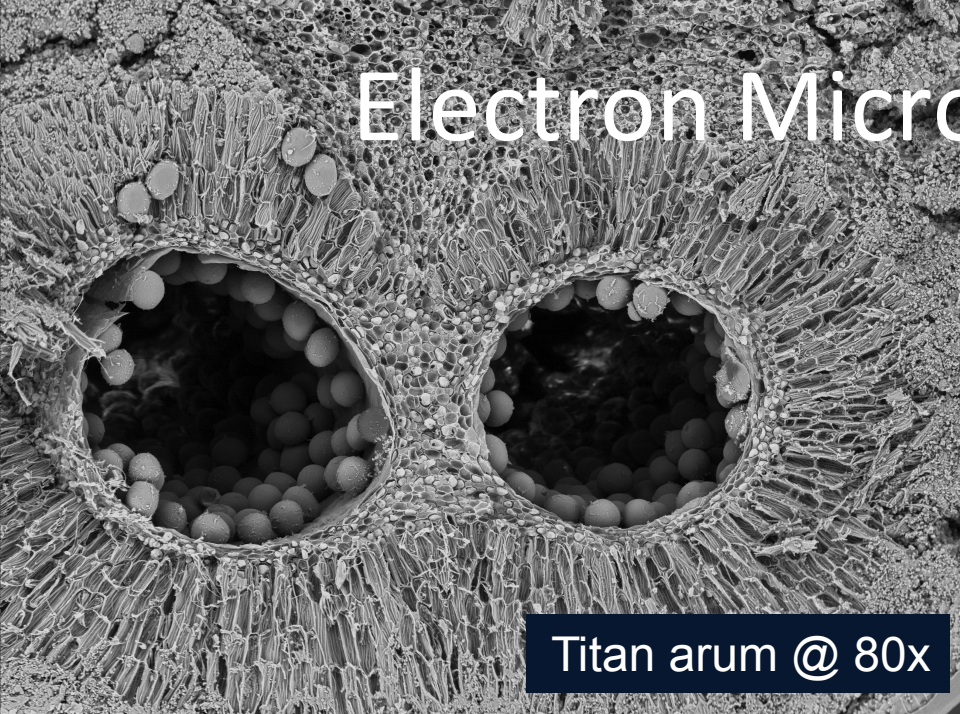


- Many engineering efforts to reduce collection time

(Lichtman et al. @ Harvard)

Briggman and Denk, 2006, "Towards neural circuit reconstruction with volume electron microscopy techniques"

Electron Microscopy Images



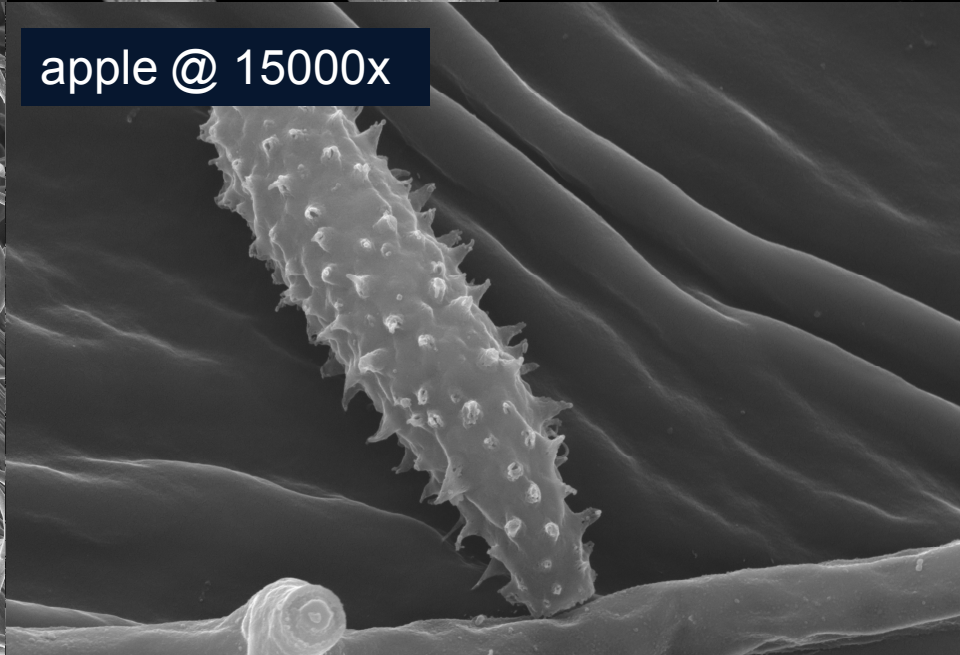
Titan arum @ 80x



Hawaiian volcanic sand @ 30x



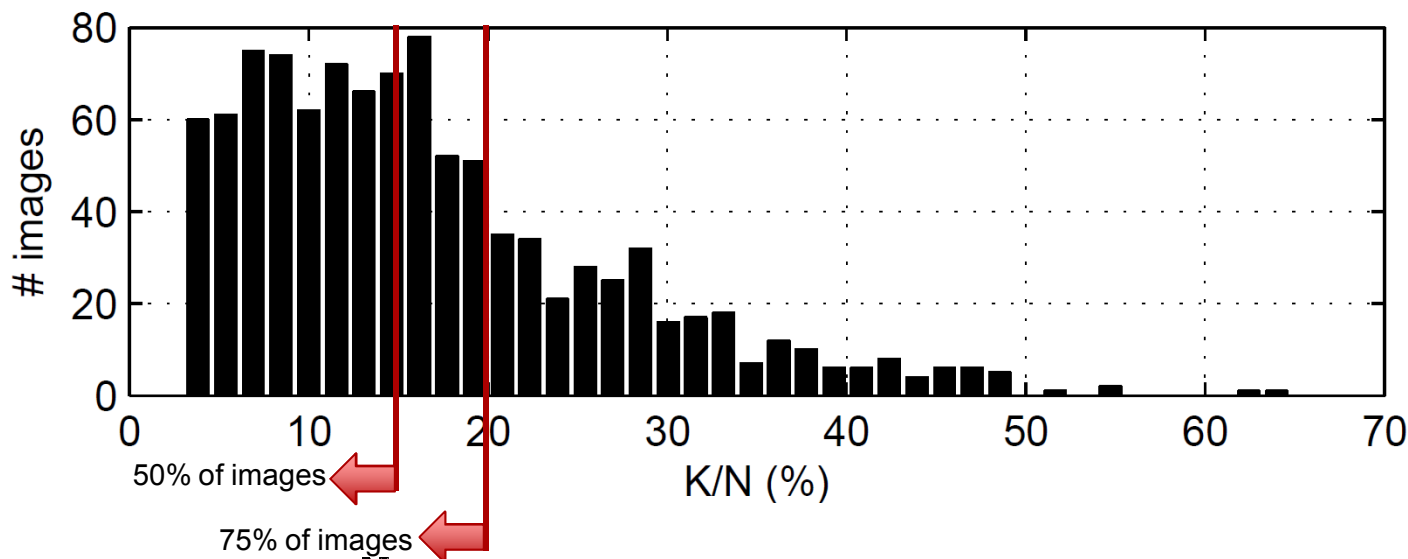
sage @ 200x



apple @ 15000x

SEM Image Compressibility

- Compression basis: block-DCT (similar to JPEG)
- K = # of coefficients required to capture at least 99.75% of image energy
- N = # of image pixels



- $M \geq O(K \log \frac{N}{K})$ # of measurements for recovery by CS

Images courtesy of Dartmouth public domain gallery: <http://www.dartmouth.edu/~emlab/gallery>

Previous Work

- Visit a random subset of pixel locations (Φ a subset of \mathbf{I})
- Measurement model: $\mathbf{y} = \Phi \mathbf{x} + \mathbf{n}$ $E(\mathbf{n}\mathbf{n}^T) = \sigma^2 \mathbf{I}$
- From $M < N$ measurements, reconstruct via

$$\begin{aligned} \min_{\mathbf{x}} \quad & \|\Psi^T \mathbf{x}\|_1 + \|\nabla \mathbf{x}\|_1 \\ \text{s.t.} \quad & \|\mathbf{y} - \Phi \mathbf{x}\| \leq \sigma^2 \end{aligned}$$

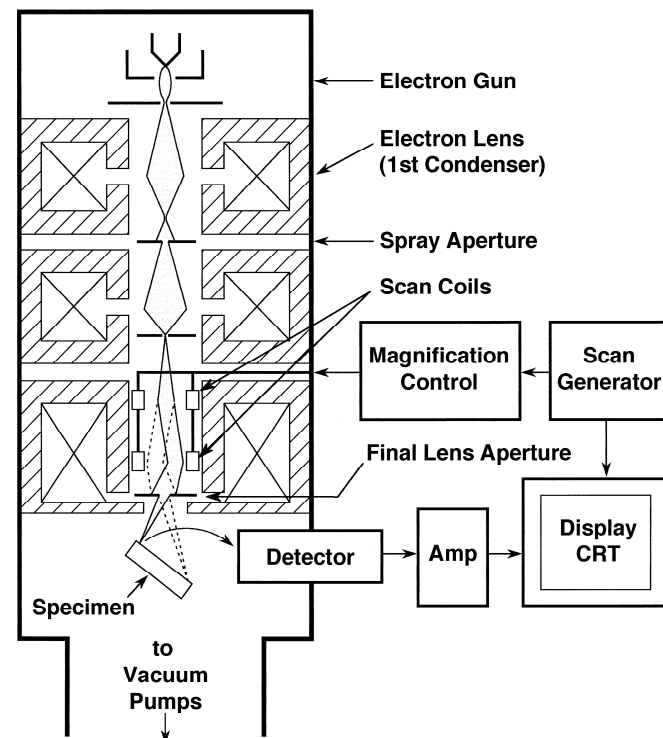
- Compression basis Ψ chosen to be block-DCT
 - Good compressibility of SEM images
 - Low mutual coherence
- Total variation regularizer $\|\nabla \mathbf{x}\|_1$ to denoise and promote smoothness between block boundaries

Scan coil dynamics

- Electron probe positioned via electromagnetic coils

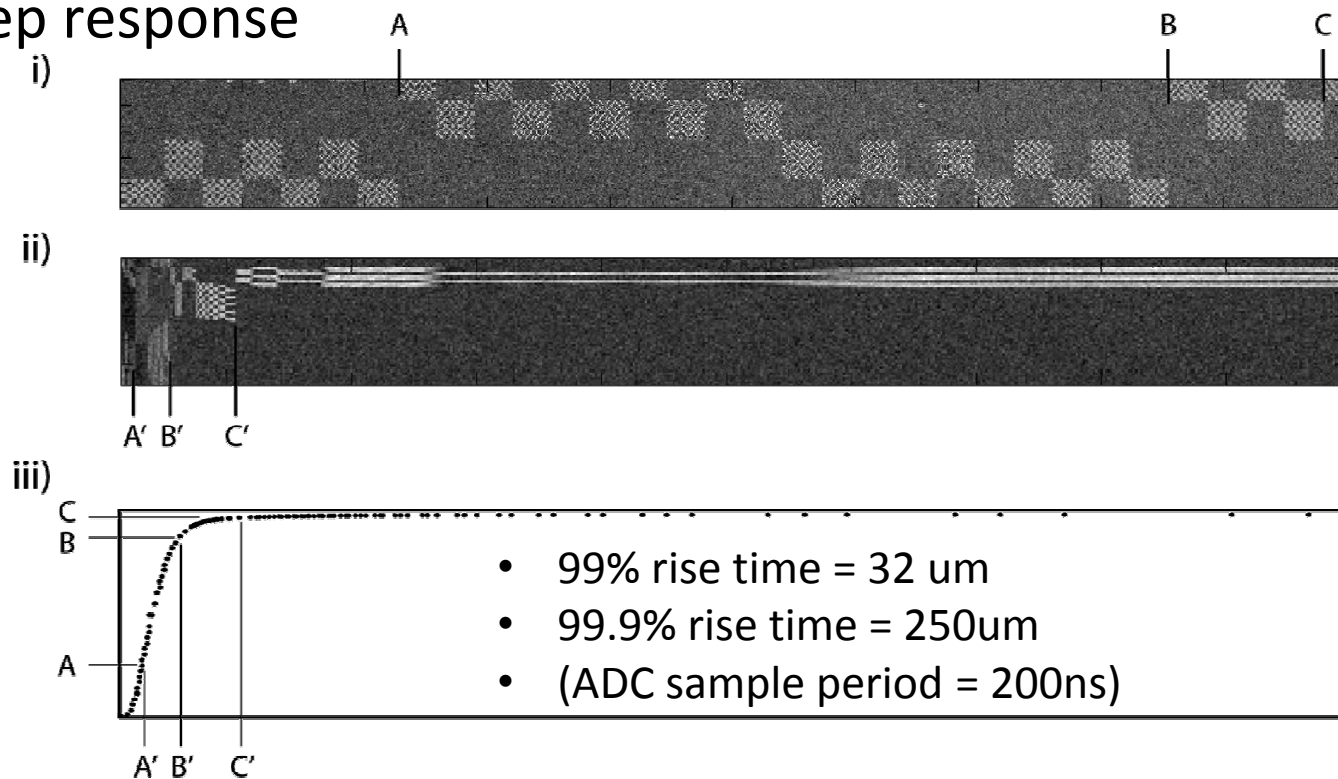
$$\mathbf{F} = q [\mathbf{E} + (\mathbf{v} \times \mathbf{B})]$$

- Slow compared to sample period
- Commanded position \neq actual position
 - Transient delay
 - Steady state lag



Scan coil dynamics

■ Measure step response



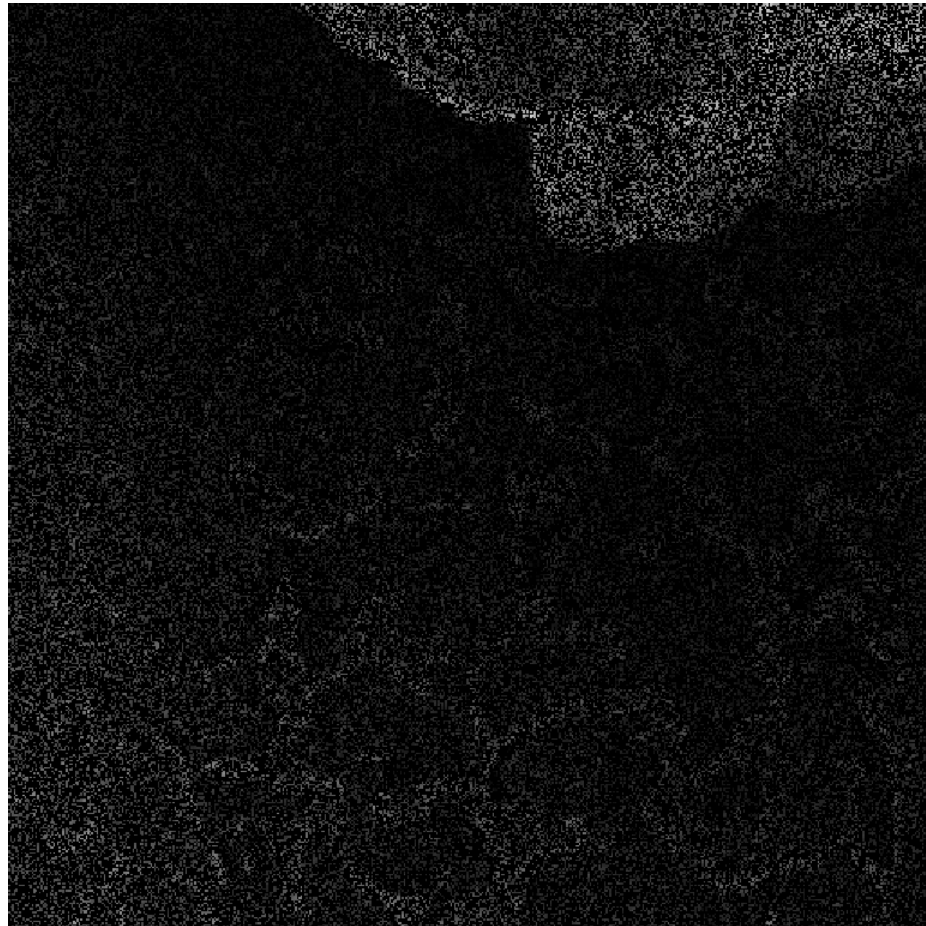
■ Linear dynamical model to predict “actual” location

$$\frac{d^5 x(t)}{dt^5} = a_0(\hat{x}(t) - x(t)) - a_1 \frac{dx(t)}{dt} - a_2 \frac{d^2 x(t)}{dt^2} - a_3 \frac{d^3 x(t)}{dt^3} - a_4 \frac{d^4 x(t)}{dt^4}$$

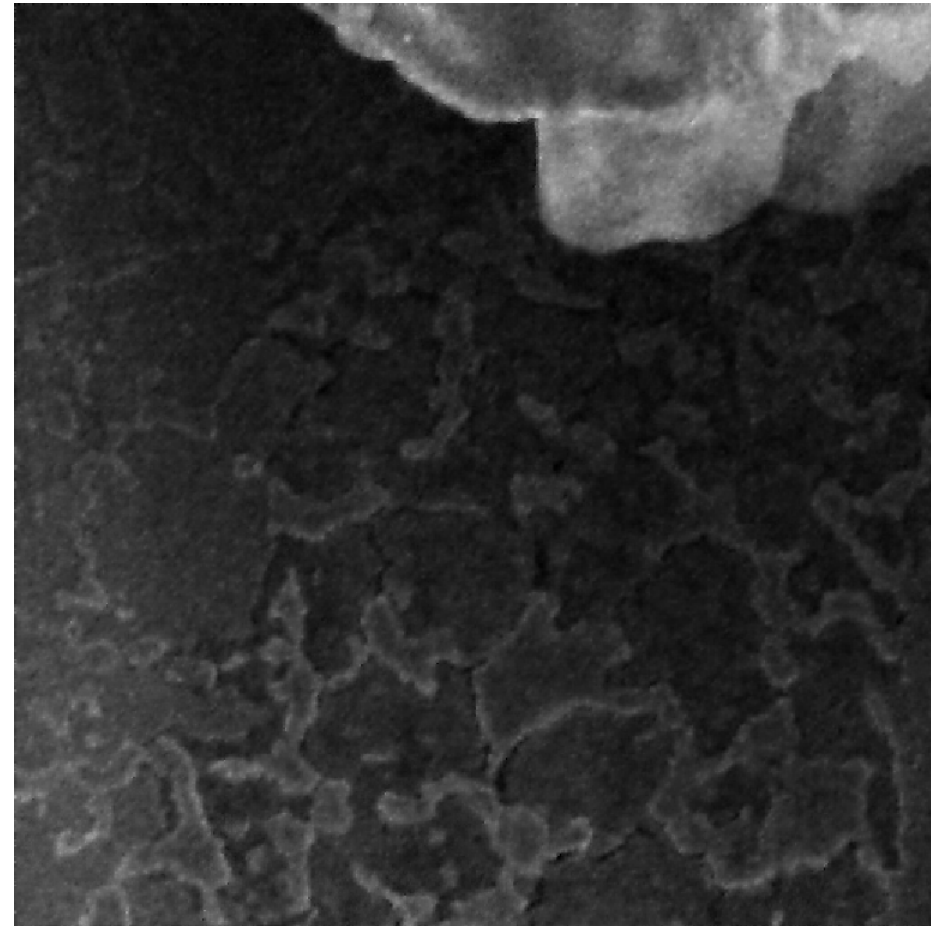
Simulated: Gibeon meteorite surface

(noiseless simulated recover)

$M/N = 30\%$



recovered

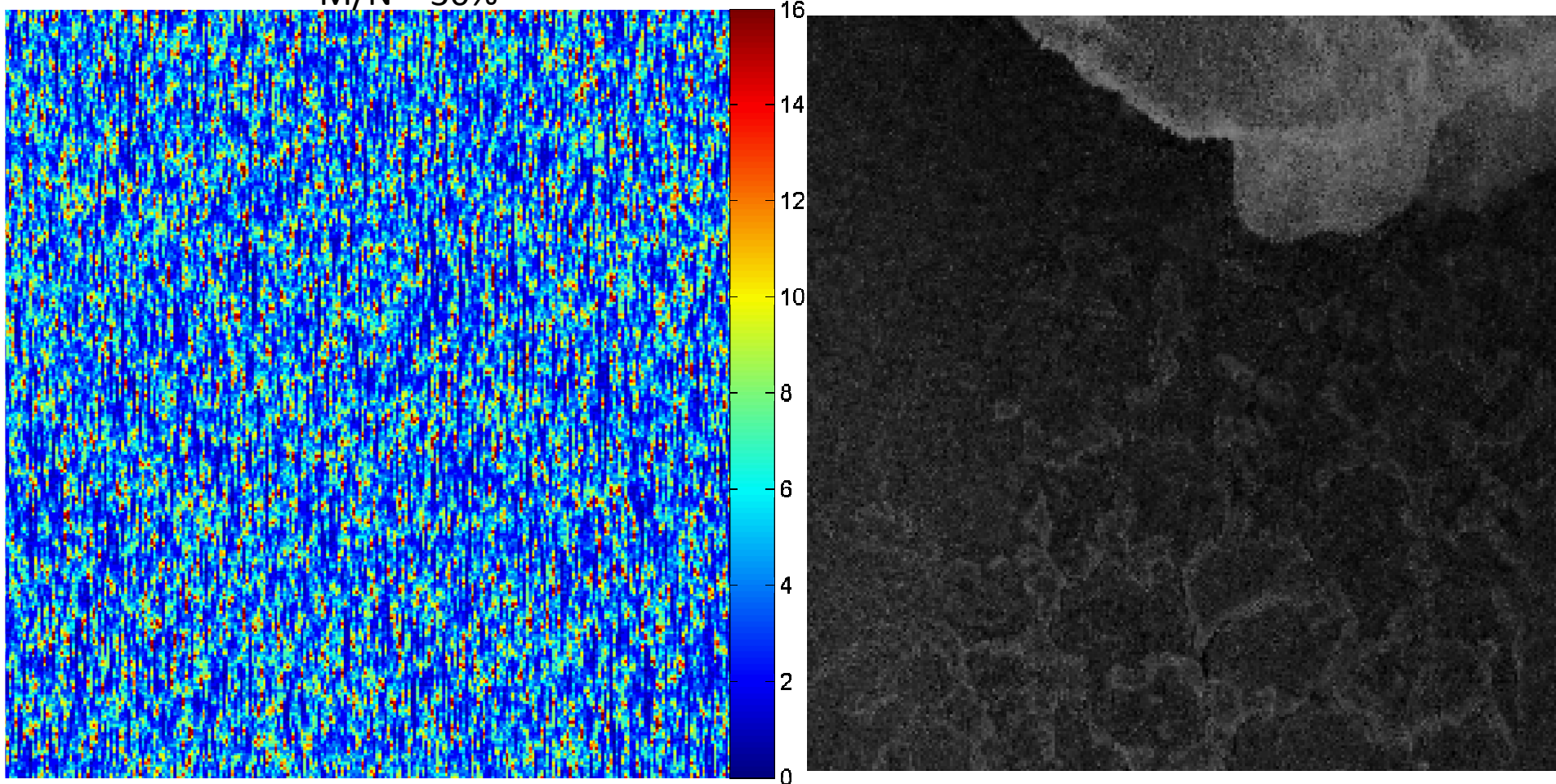


Actual: Gibeon meteorite surface

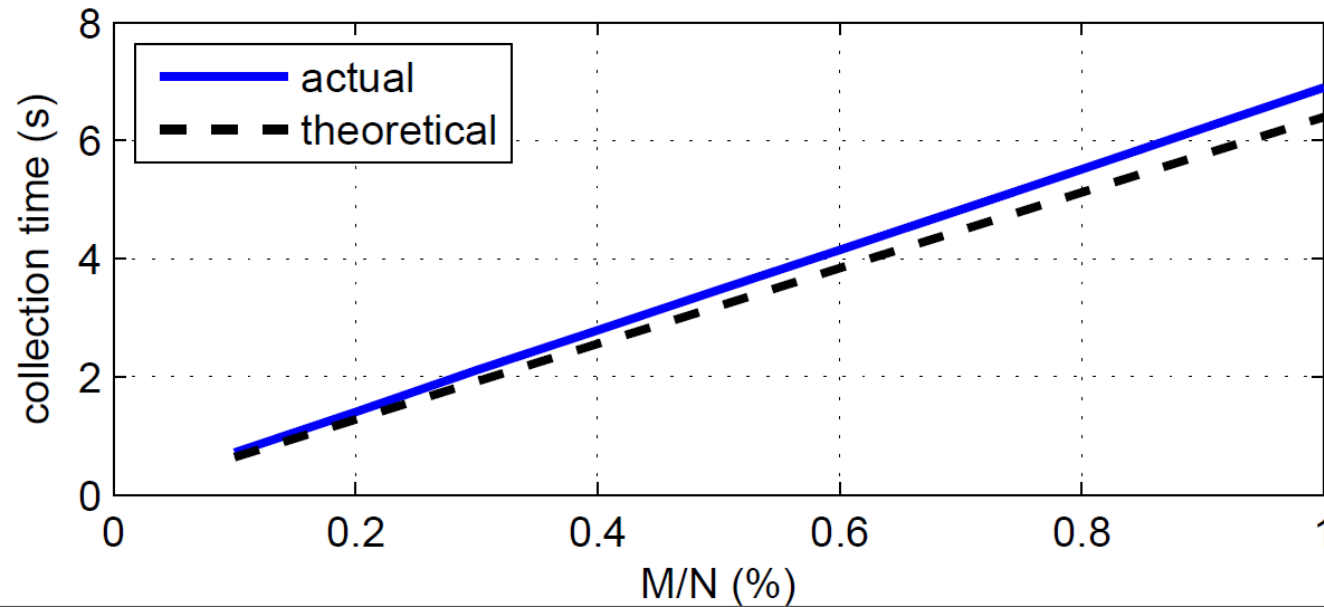
(actual measurement location + recovery)

M/N = 30%

recovered



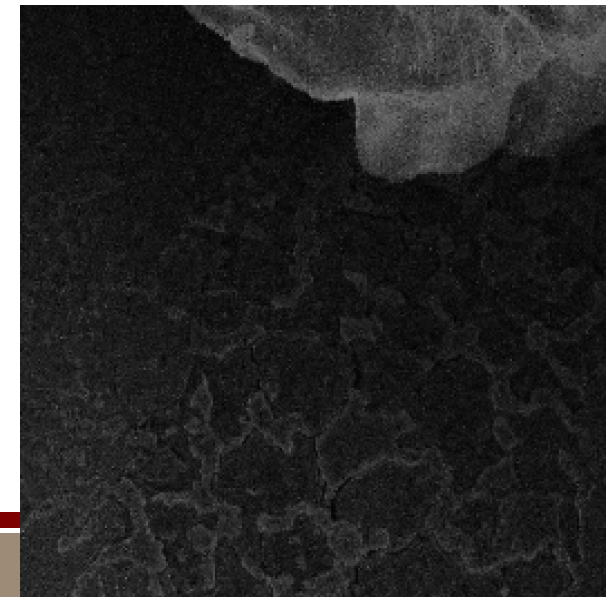
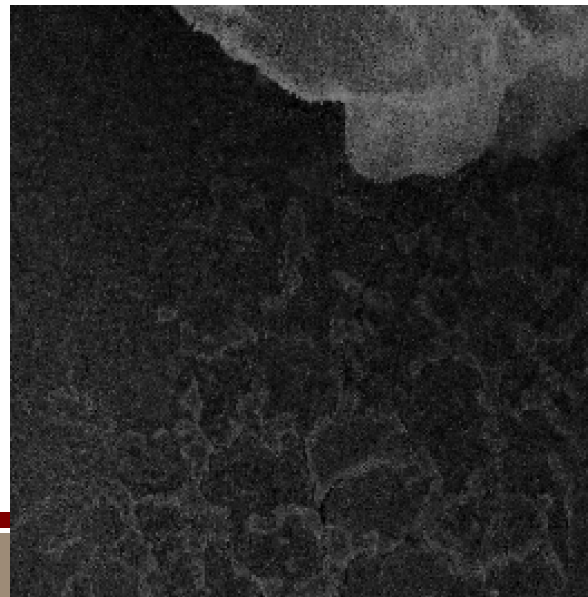
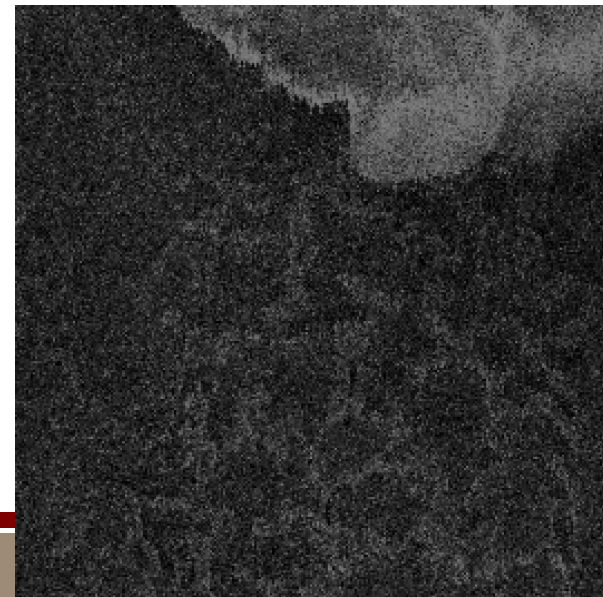
Undersampling timing results



$M/N = 10\%$

$M/N = 30\%$

$M/N = 50\%$




Sparse sampling summary

- Preliminary demonstration of sparse sampling & reconstruction in an operational SEM
- Acceptable image quality at 2-3x speedup
- Speedups **in series** with other engineering advances

Shortcomings:

- Requires ~10x more time to reconstruct data than to collect
- Only viable for “smooth” images (compressible by block-DCT)

Outline

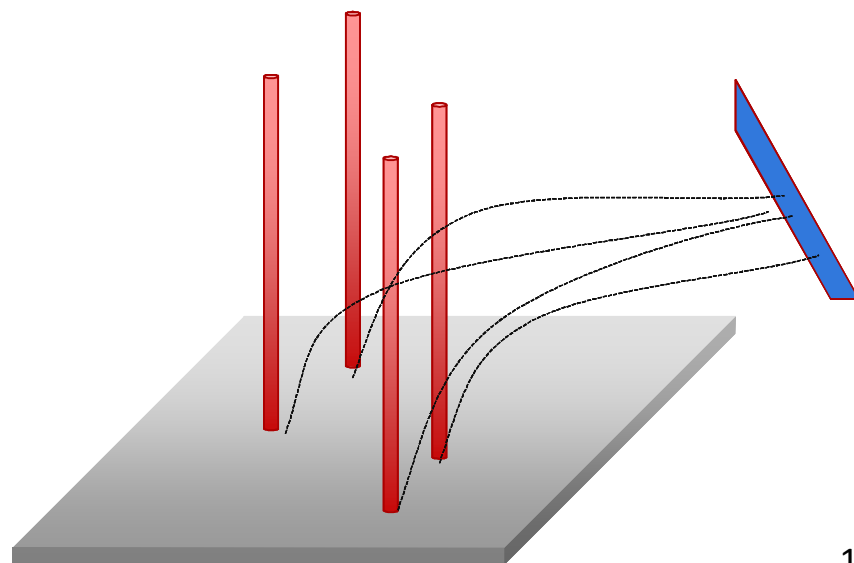
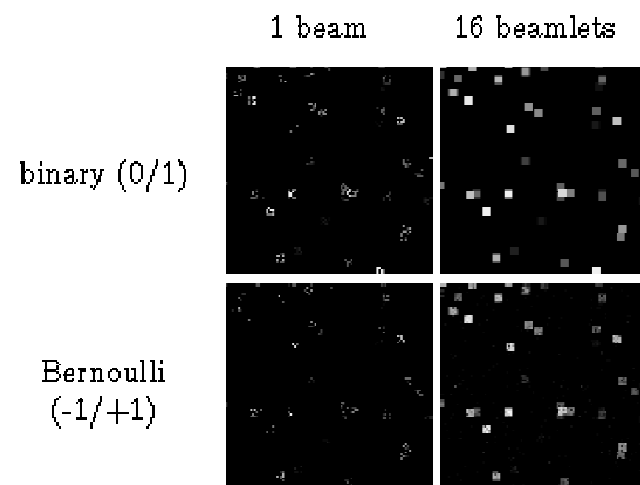
- Background and Motivation
- Previous work: sparse sampling an operational SEM
-  ■ Analysis of multi-beam measurements
- Summary

Multiple beams, single detector

Multiplexed measurements enable reconstructing
broader class of images

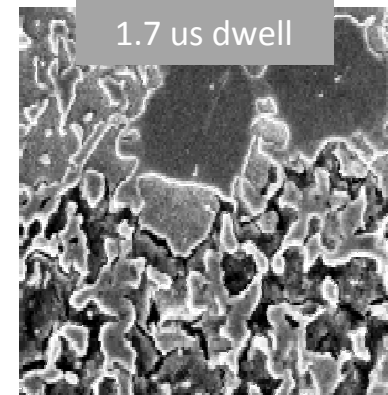
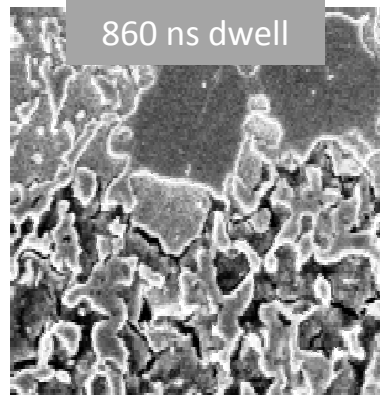
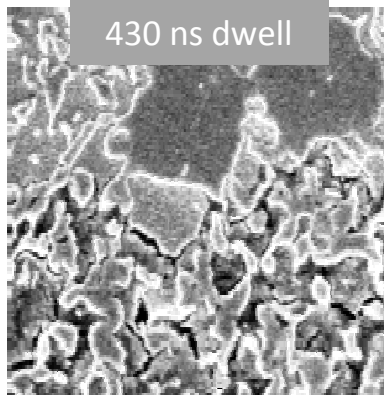
Hypothetical multibeam tool:

- Multi-beam source projects sparse, programmable pattern on the sample
- Single detector with linear response and sufficient dynamic range



Experimental setup

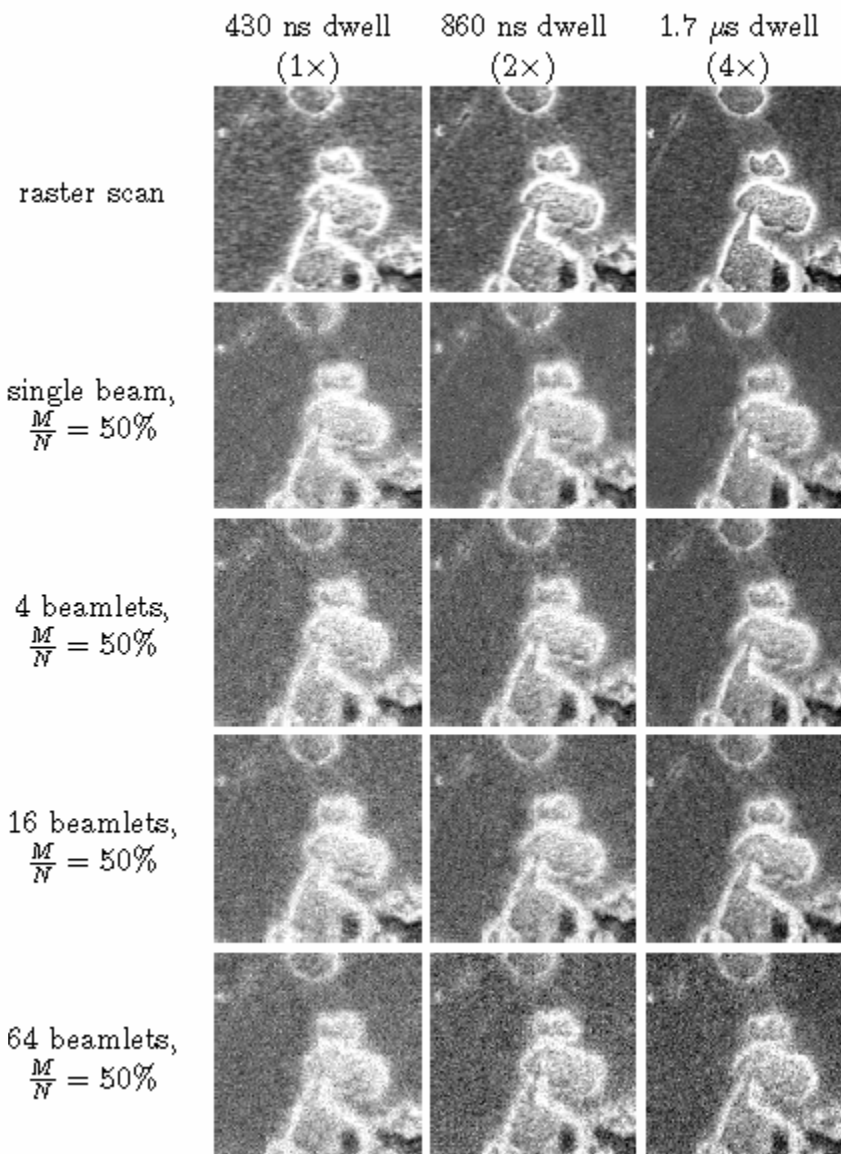
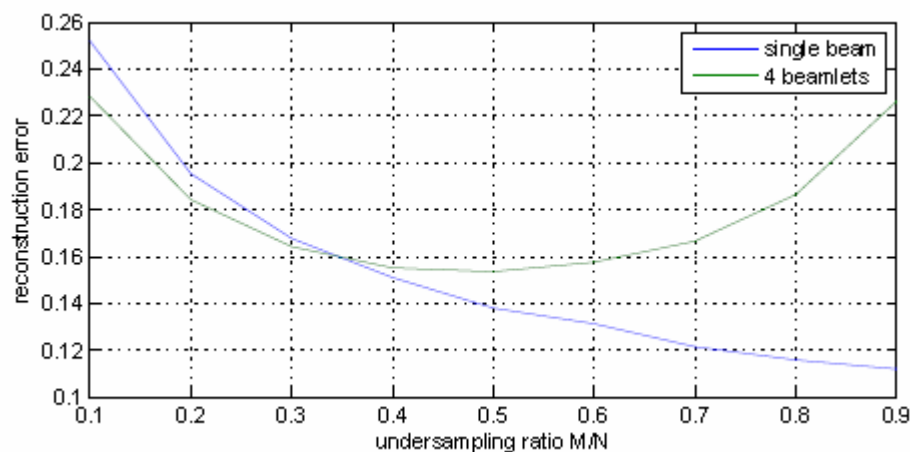
- Commercially available SEM column from Zeiss GmbH
 - Schottky thermal field emission source
 - Nominal beam energy of 10 kEV, 10 μm aperture, ~ 200 pA beam
 - Secondary electron detector
- Collect 1000 800x800-pixel images of single area of interest
 - Register image stack after collection to compensate for drift



- Synthesize multibeam measurements in software
 - Simple sum of responses from selected pixels, adds intensity + noise
 - Assumes (incorrectly) no detector noise

Results

- Using a few beamlets
 - Provides moderate quality improvement over sparse imaging for “large” M/N (50%)



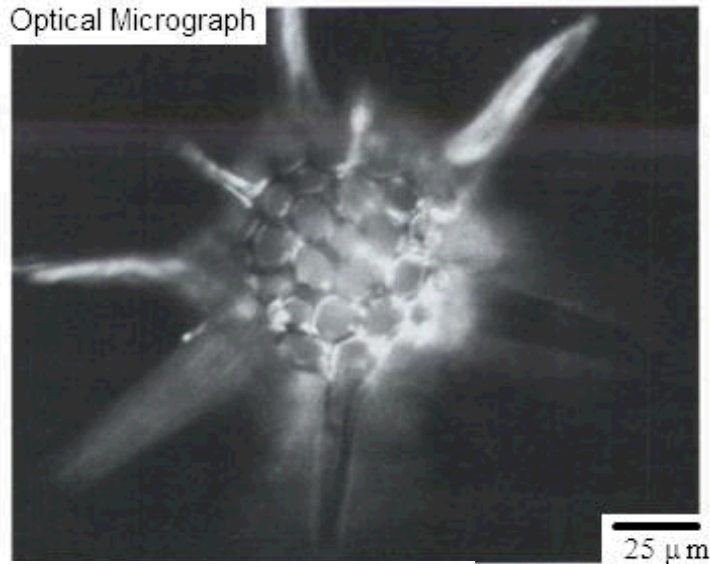
- **Single-beam sparse sampling:**
 - acceptable image quality at 2-3x speedup
 - speedups **in series** with other engineering advances
 - **demonstrated in operational tool**
 - Doesn't generalize to non-smooth images

- **Multibeam compressed sampling:**
 - Possibly provides modest quality improvement over sparse sampling for speedup of $\sim 2x$ or less
 - Generalizes to non-smooth images
 - Synthetic multibeam measurements lack appropriate noise conditions, optimistic in some settings (linear detector), pessimistic in others (detector noise)

[backup slides]

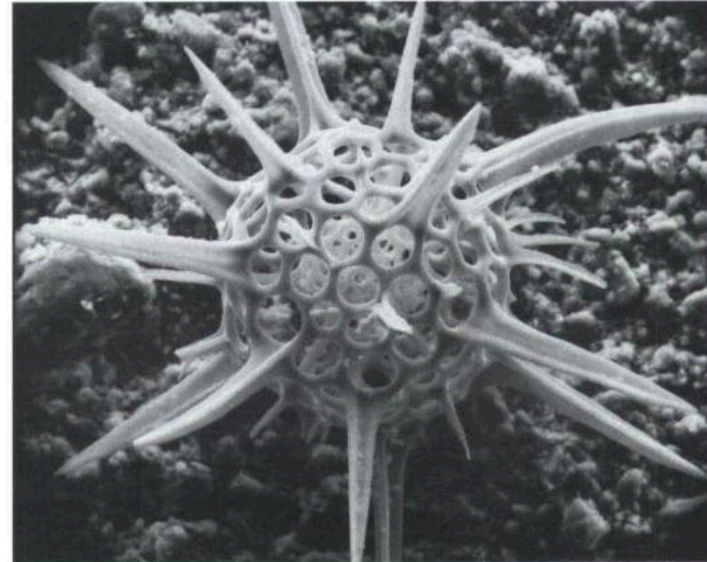
Why SEM?

Optical Microscope Image



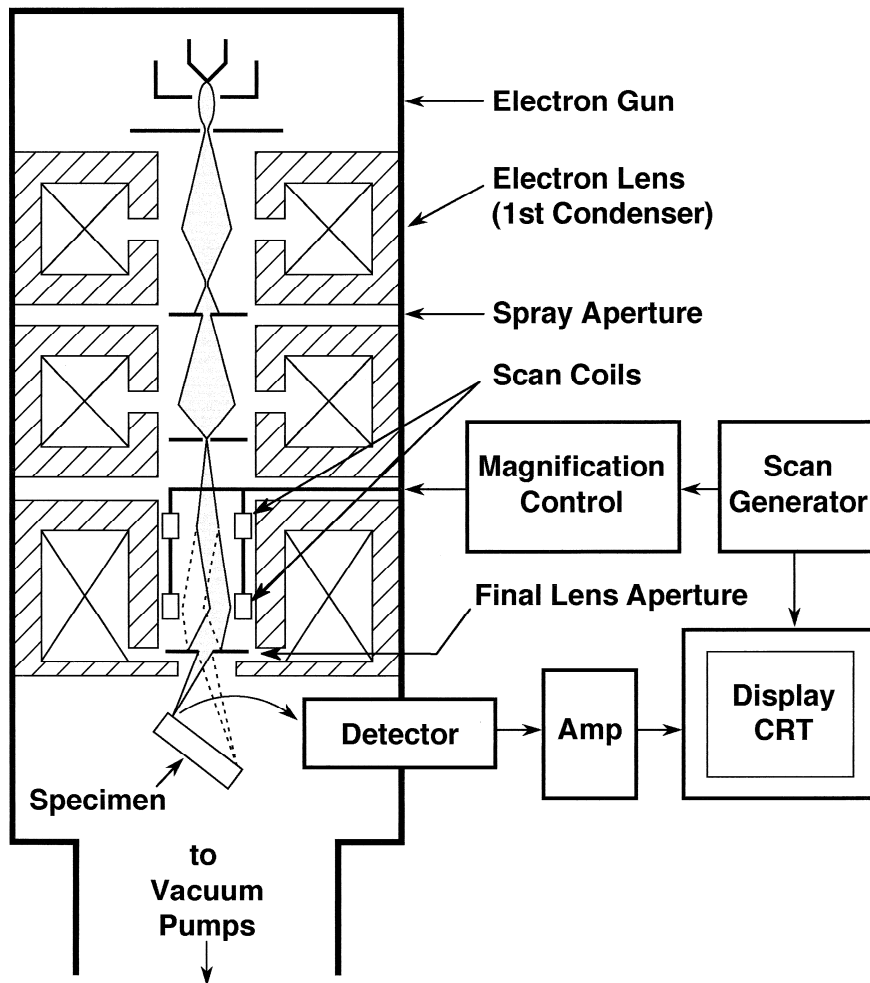
Radiolarian (marine organism)

SEM Image



- Typical SEMs can resolve ~ 1 nm features ($10^3\times$ smaller diff. limit than optical)
- Large depth of focus
- Flexible viewing conditions, e.g., 10x to 500,000x mag

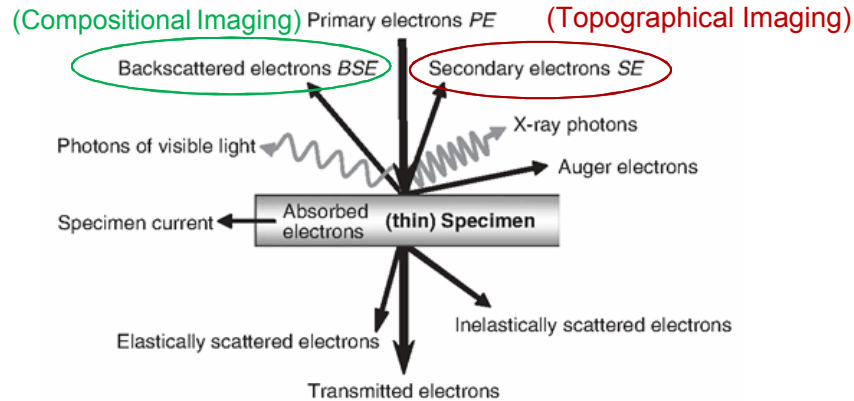
SEM Electron Column



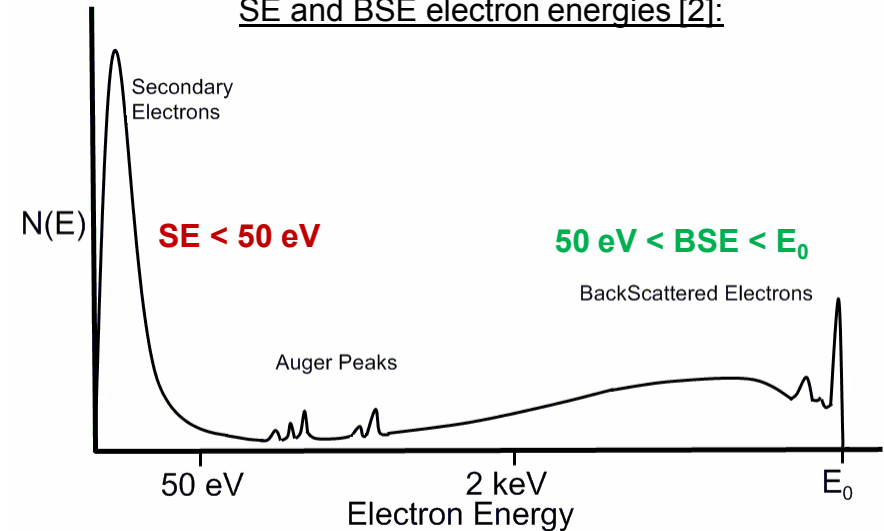
- Electron gun generates electrons
- Electromagnetic condenser lenses and apertures focus electrons into a beam w/ small spot size (~1 nm)
- Scan coils raster beam across sample area to be images
- Detector collects electrons at each point of raster pattern and plots on computer display (typically a single SE/BSE, but there may be other, specialized detectors).

Interaction of Electrons with Solids

Probe/sample interactions [1]:



SE and BSE electron energies [2]:

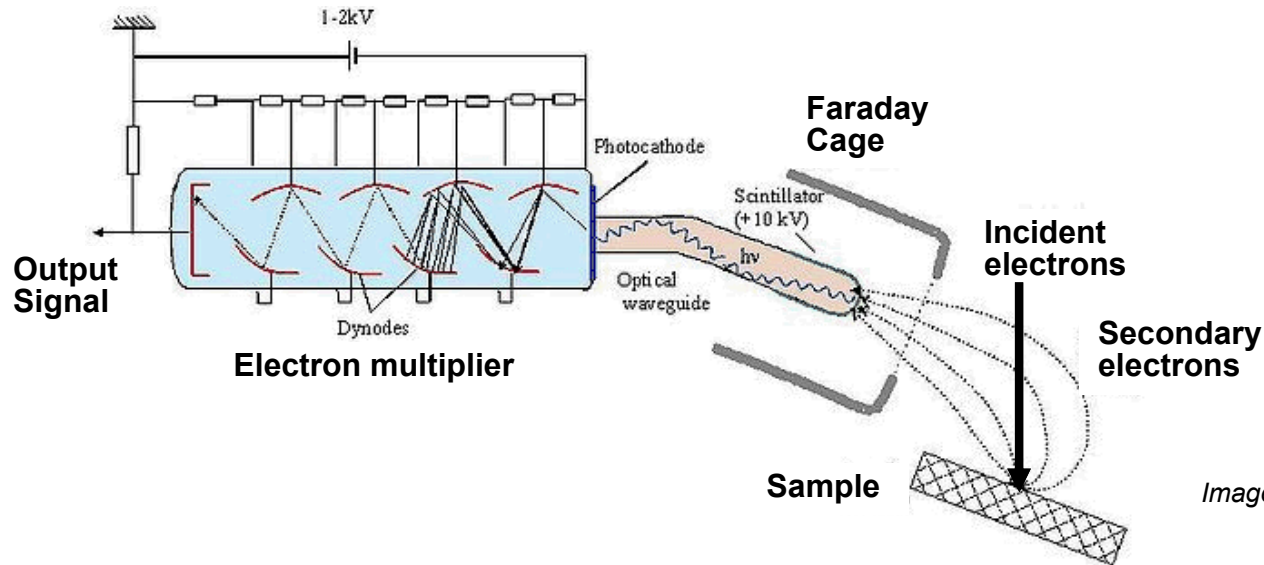


- Electron interaction with a solid results in a number of processes
- SEM uses scattered electrons for sample imaging
- Backscattered electrons (BSEs):
 - elastic collisions with atoms nuclei
 - high energy => heavily influenced by atomic number of material (He $Z=2$, Au $Z=79$)
- Secondary electrons (SEs):
 - weakly bound electrons excited from the sample
 - low energy => heavily influenced by surface topography

[1] D..J. Stokes, *Principles and Practice of Variable Pressure/Environments Scanning Electron Microscopy* (John Wiley & Sons, Ltd., UK, 2008).

[2] From J. Mabon, *SEM and FIB in Materials Research*, UIUC

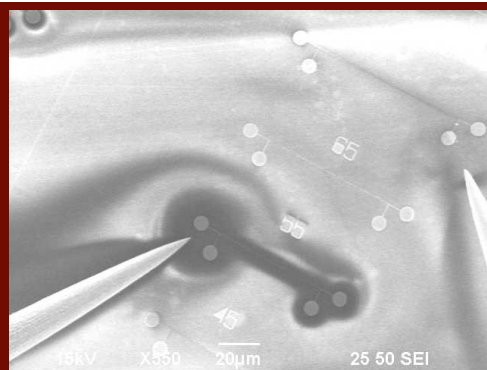
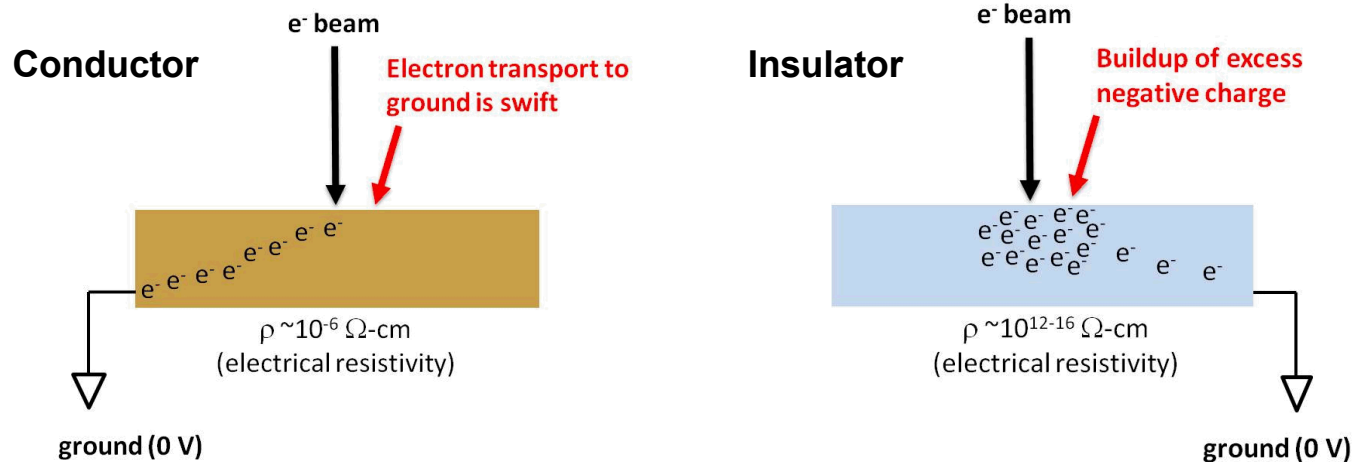
Collection of Scattered Electrons



- Everhart-Thornley (E-T) detectors are the most widely used detectors in SEM. Can measure both backscattered electrons (BSE) and secondary electrons (SE).
- Bias voltage on Faraday cage & scintillator selects between BSE and SE. This is small compared to the primary beam (~few hundred V).
- Electron that passes Faraday cage strikes a scintillator, which converts the signal to light that is directed down an optical waveguide
- The light signal is converted back to electrons (at photocathode), which is amplified by an electron multiplier (gain $\sim 10^5$ - 10^6) and collected by software

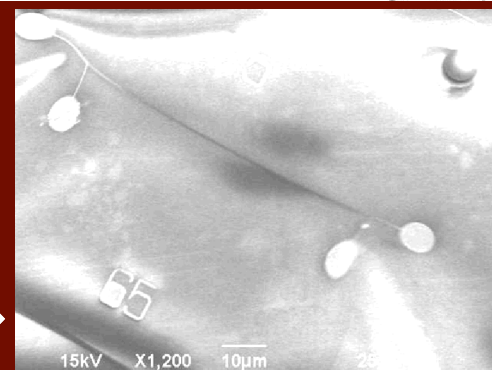
Challenge #2: sample charging

- Charging: electron buildup in sample with no path-to-ground
- Causes image distortion: Surface potential large enough to deflect electrons incident to or reflected from the sample



Grounded
by electrical
probe

No path to
ground

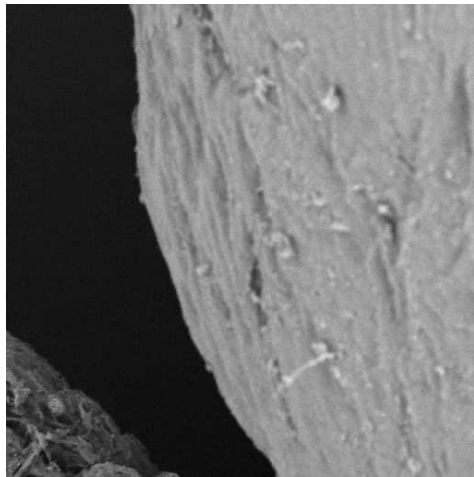


Images courtesy of the
Technical University of Graz
(Graz, Austria)

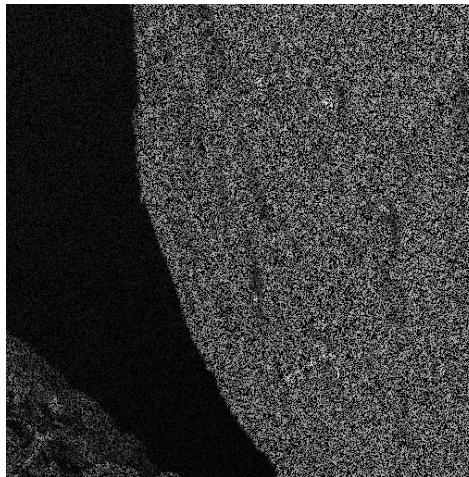
source:
<http://lamp.tu-graz.ac.at/~hadley/sem/charging/charging.php>

Sparse reconstruct example

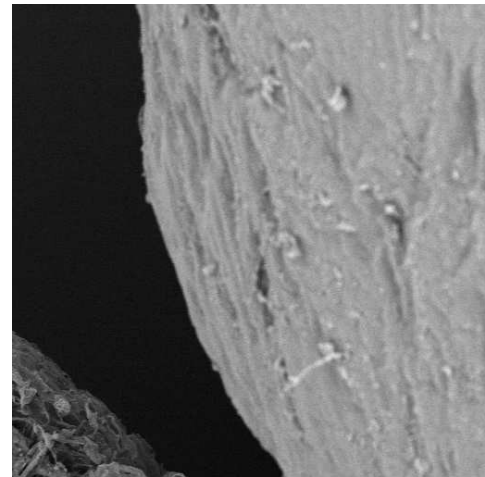
- Interpolation + denoising using block-DCT with TV regularizer



original



50% samples



reconstruction (36 dB PSNR)

- What about simpler/more efficient bilinear interpolation?
(more efficient, but brittle to noise)

Implementation

- Solve efficiently via split Bregman method (Goldstein & Osher, 2009)

(unconstrained) $\min_{\mathbf{x}} \|\Psi^T \mathbf{x}\|_1 + \|\nabla \mathbf{x}\|_1 + \frac{\mu}{2} \|\mathbf{y} - \Phi \mathbf{x}\|_2^2$

solve for image and auxiliary variables:

$$\min_{\mathbf{x}, \mathbf{u}, \mathbf{v}, \mathbf{w}} \|\mathbf{w}\|_1 + \|(\mathbf{u}, \mathbf{v})\|_2 + \frac{\mu}{2} \|\Phi \mathbf{x} - \mathbf{y}\|_2^2 \\ + \frac{\lambda}{2} \|\mathbf{u} - \nabla_u \mathbf{x} - \mathbf{b}_u^k\|_2^2 + \frac{\lambda}{2} \|\mathbf{v} - \nabla_v \mathbf{x} - \mathbf{b}_v^k\|_2^2 + \frac{\gamma}{2} \|\mathbf{w} - \Psi^T \mathbf{x} - \mathbf{b}_w^k\|_2^2.$$

update Bregman parameters

$$\mathbf{b}_u^{k+1} = \mathbf{b}_u^k + \left(\nabla_u \mathbf{x}^{k+1} - \mathbf{u}^{k+1} \right)$$

$$\mathbf{b}_v^{k+1} = \mathbf{b}_v^k + \left(\nabla_v \mathbf{x}^{k+1} - \mathbf{v}^{k+1} \right)$$

$$\mathbf{b}_w^{k+1} = \mathbf{b}_w^k + \left(\Psi^T \mathbf{x}^{k+1} - \mathbf{w}^{k+1} \right)$$

Implementation

$$\min_{\mathbf{x}, \mathbf{u}, \mathbf{v}, \mathbf{w}} \|\mathbf{w}\|_1 + \|(\mathbf{u}, \mathbf{v})\|_2 + \frac{\mu}{2} \|\Phi \mathbf{x} - \mathbf{y}\|_2^2 \\ + \frac{\lambda}{2} \|\mathbf{u} - \nabla_u \mathbf{x} - \mathbf{b}_u^k\|_2^2 + \frac{\lambda}{2} \|\mathbf{v} - \nabla_v \mathbf{x} - \mathbf{b}_v^k\|_2^2 + \frac{\gamma}{2} \|\mathbf{w} - \Psi^T \mathbf{x} - \mathbf{b}_w^k\|_2^2$$

■ Alternating minimizations

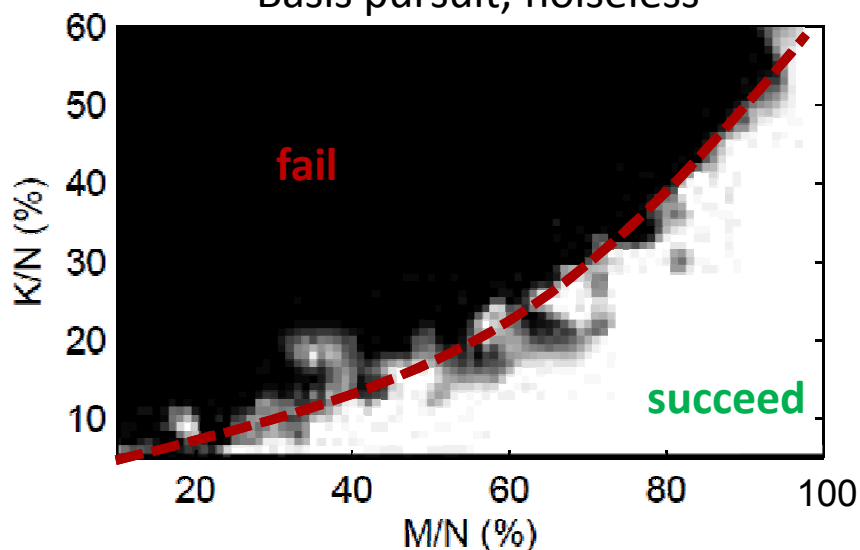
- Efficient solution for $\mathbf{w}, \mathbf{u}, \mathbf{v}$ via elementwise shrinkage
- Efficient (inexact) solution to \mathbf{x} via Fourier (circulant approx)

diagonal
(non-constant) circulant

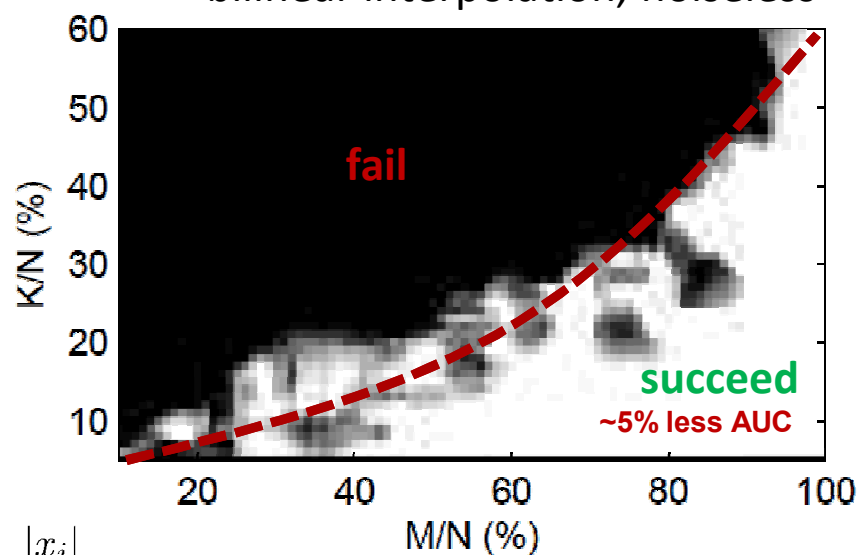
$$((\mu \Phi^T \Phi) - (\lambda \Delta + \gamma \mathbf{I})) \mathbf{x} = \mu \Phi^T \mathbf{y} + \lambda \nabla_u^T (\mathbf{u}^k - \mathbf{b}_u) + \lambda \nabla_v^T (\mathbf{v}^k - \mathbf{b}_v) + \gamma \Psi (\mathbf{w}^k - \mathbf{b}_w)$$

Phase transition curves

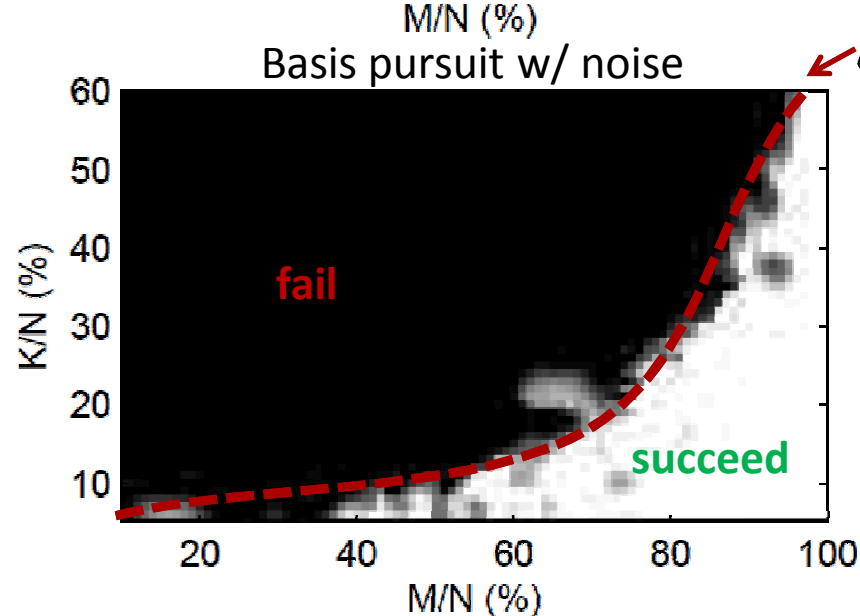
Basis pursuit, noiseless



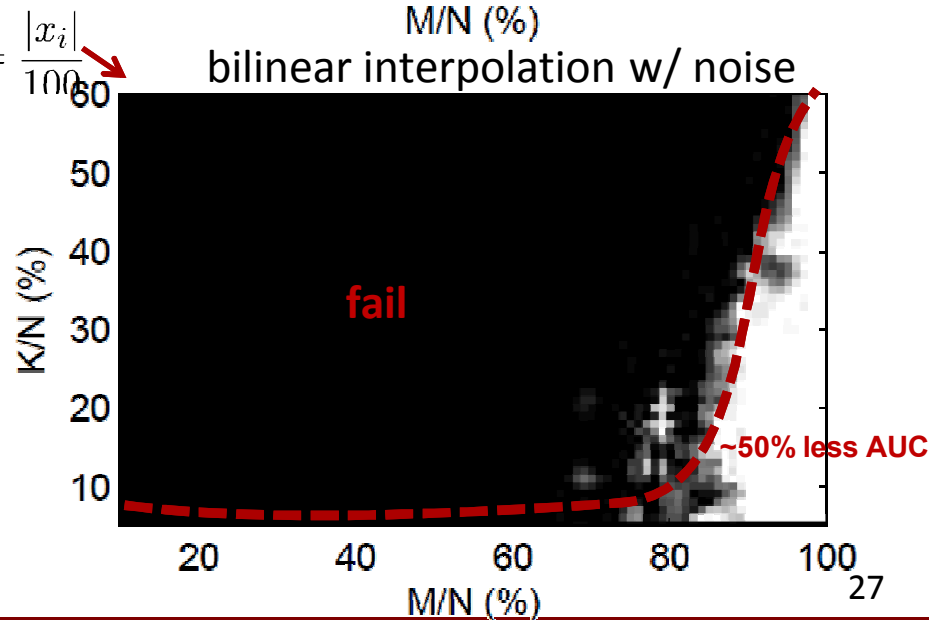
bilinear interpolation, noiseless



Basis pursuit w/ noise



bilinear interpolation w/ noise



$$\sigma_i^2 = \frac{|x_i|}{100}$$