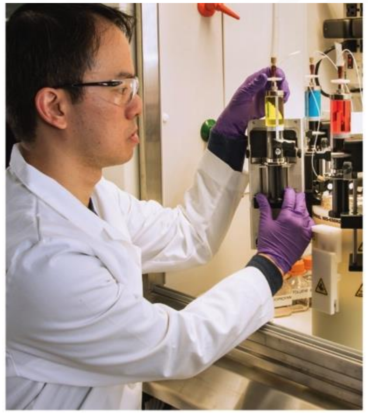
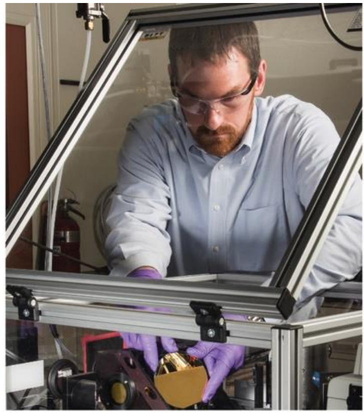




Computational Frontiers in Microscopy and Microanalysis

Or, when “making up data” might actually be okay…

Joshua Taillon

September 15, 2017

NIST
National Institute of Standards and Technology
U.S. Department of Commerce

MATERIAL MEASUREMENT LABORATORY

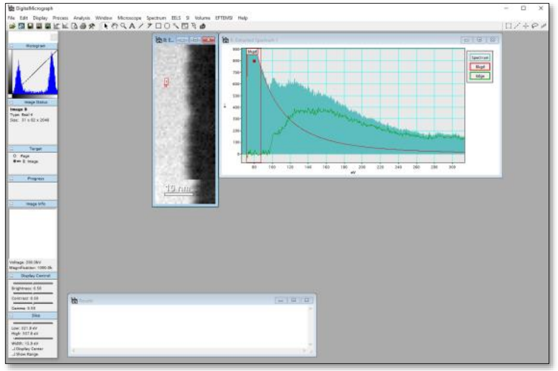
Disclaimer

Certain commercial equipment, instruments, materials, vendors, and software are identified in this talk for example purposes and to foster understanding. Such identification does not imply recommendation or endorsement by NIST, nor does it imply that the materials or equipment identified are necessarily the best available for the purpose.

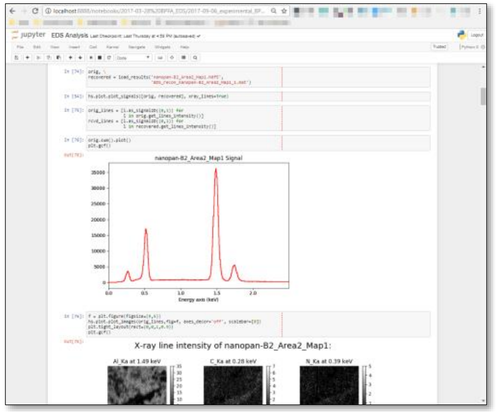
Outline

- What is "computational microscopy"
- A shifting paradigm for microscopists and microanalysts
- Introduction to and applications of compressive sensing in microscopy
- Some of our initial work

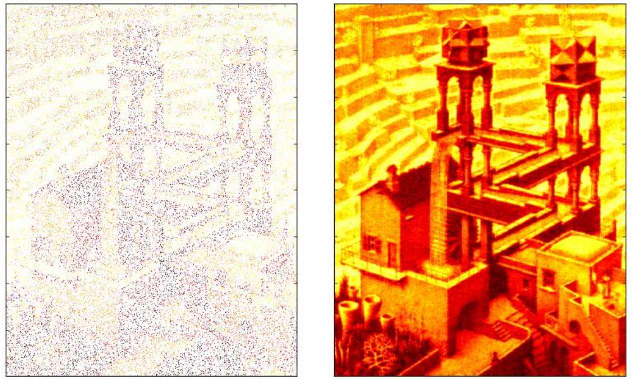
Proprietary/
interactive GUI



Open/reproducible
notebook GUI



Compressed
Sensing



http://www.pyrunner.com

Computational Microscopy

NB: This is personal opinion! Feel free to argue with me…

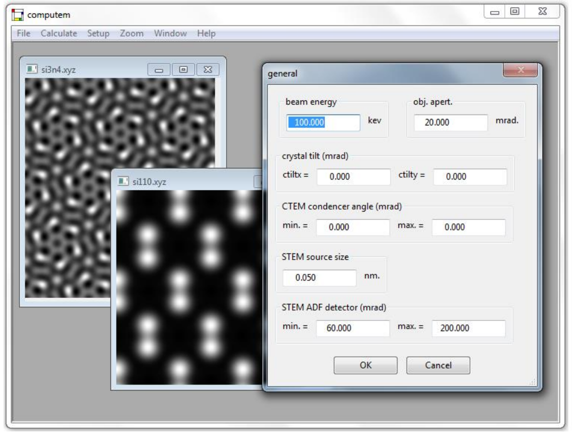
Defining “Computational Microscopy”

- **What don’t we mean?**
  - Digitization
  - Image simulation
  - Image processing/analysis

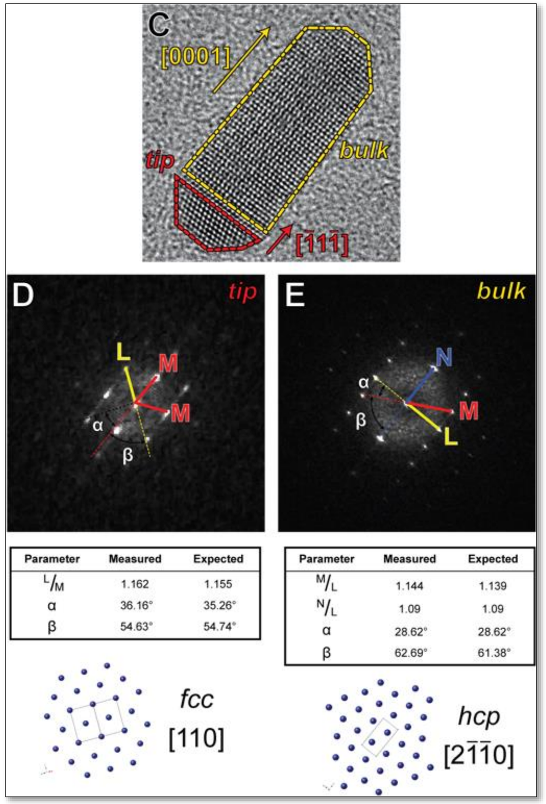
    …in the basic form…

Kodak TEM film; Ted Pella

Direct e⁻ detector; Gatan



EJ Kirkland; Multislice TEM Simulation



HRTEM Fourier analysis

Defining “Computational Microscopy”

NB: This is personal opinion! Feel free to argue with me…

- **An attempt at a definition:**

“Microscopy directed by or collected primarily for computational processes

(as opposed to by or for the user directly)”

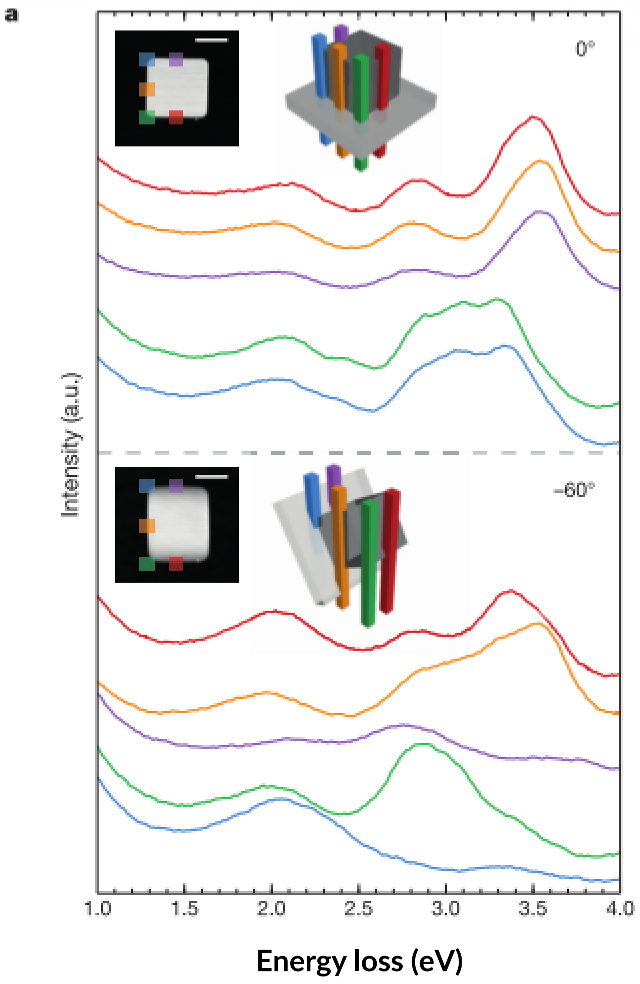
- **Relevant buzzwords:**
  - Machine learning, artificial intelligence, autonomous measurement, dynamic sampling, compressive sensing/sparse imaging

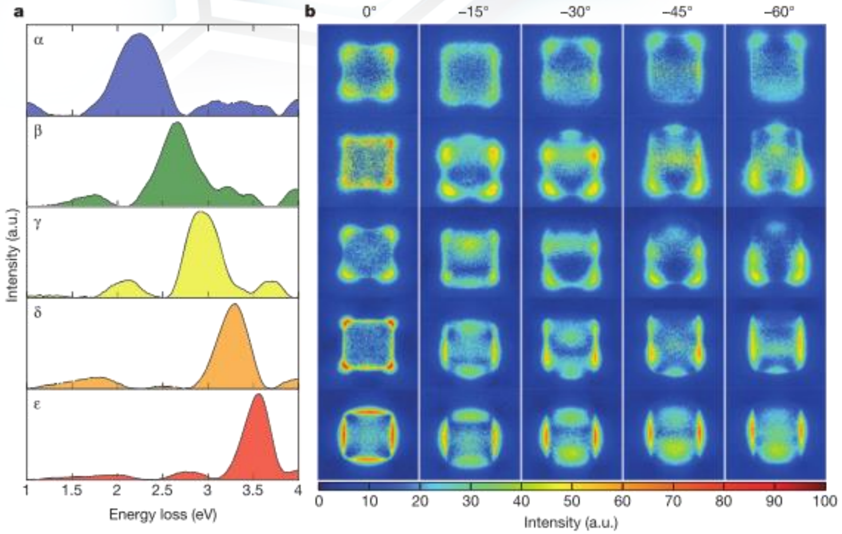
Some examples – 1/4

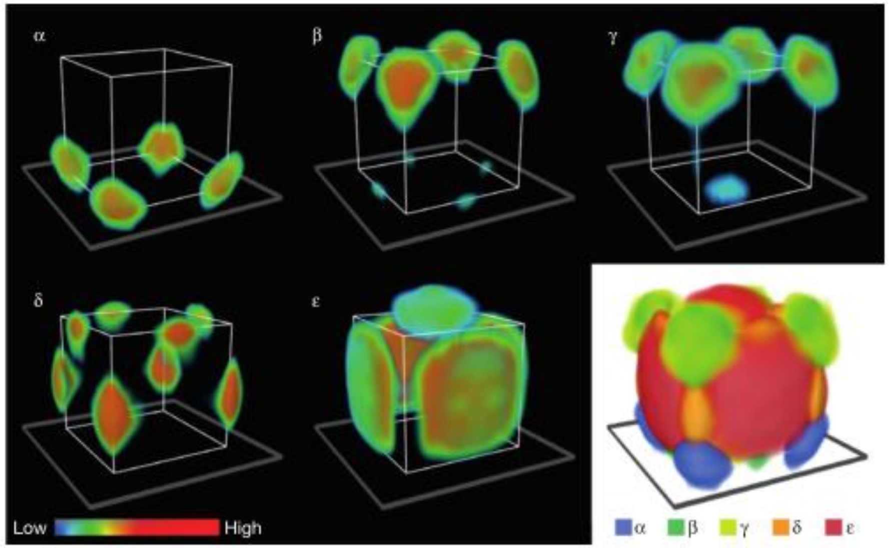
- **Machine learning factor analysis**

  O. Nicoletti, P. Midgley, *et al.*, *Nature*, 502, 80-84, 2013

- Non-negative matrix factorization of EELS spectra
- Identifying meaningful spectral components in a sea of overlapping signals
- Combine with tilt-tomography for 3D information
- Identified nanoparticle plasmon resonances







Some examples – 1/4

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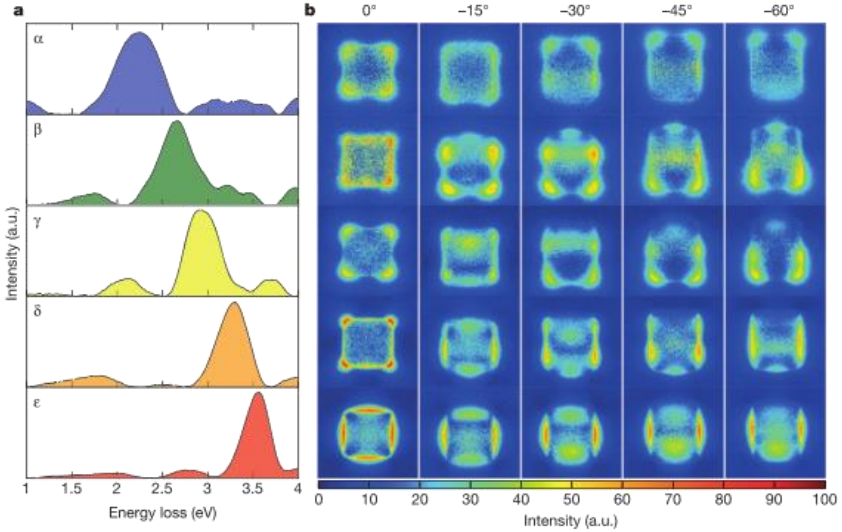
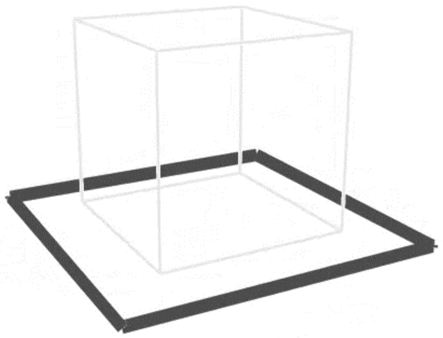
  O. Nicoletti, P. Midgley, *et al.*, *Nature*, 502, 80-84, 2013





- **Non-negative matrix factorization of EELS spectra**
- **Identifying meaningful spectral components in a sea of overlapping signals**
- **Combine with tilt-tomography for 3D information**
- **Identified nanoparticle plasmon resonances**

Some examples – 2/4

- **Dynamic sampling**

  G. Godaliyadda, C. Bouman, *et al.*, *Electronic Imaging*, 19, 1-8, 2016

- SLADS algorithm
- Sparse imaging and weighted inpainting reconstruction
- Train algorithm offline to measure how much certain types of pixels reduce overall distortion
- Online, pick new pixels to reduce expected distortion in reconstruction

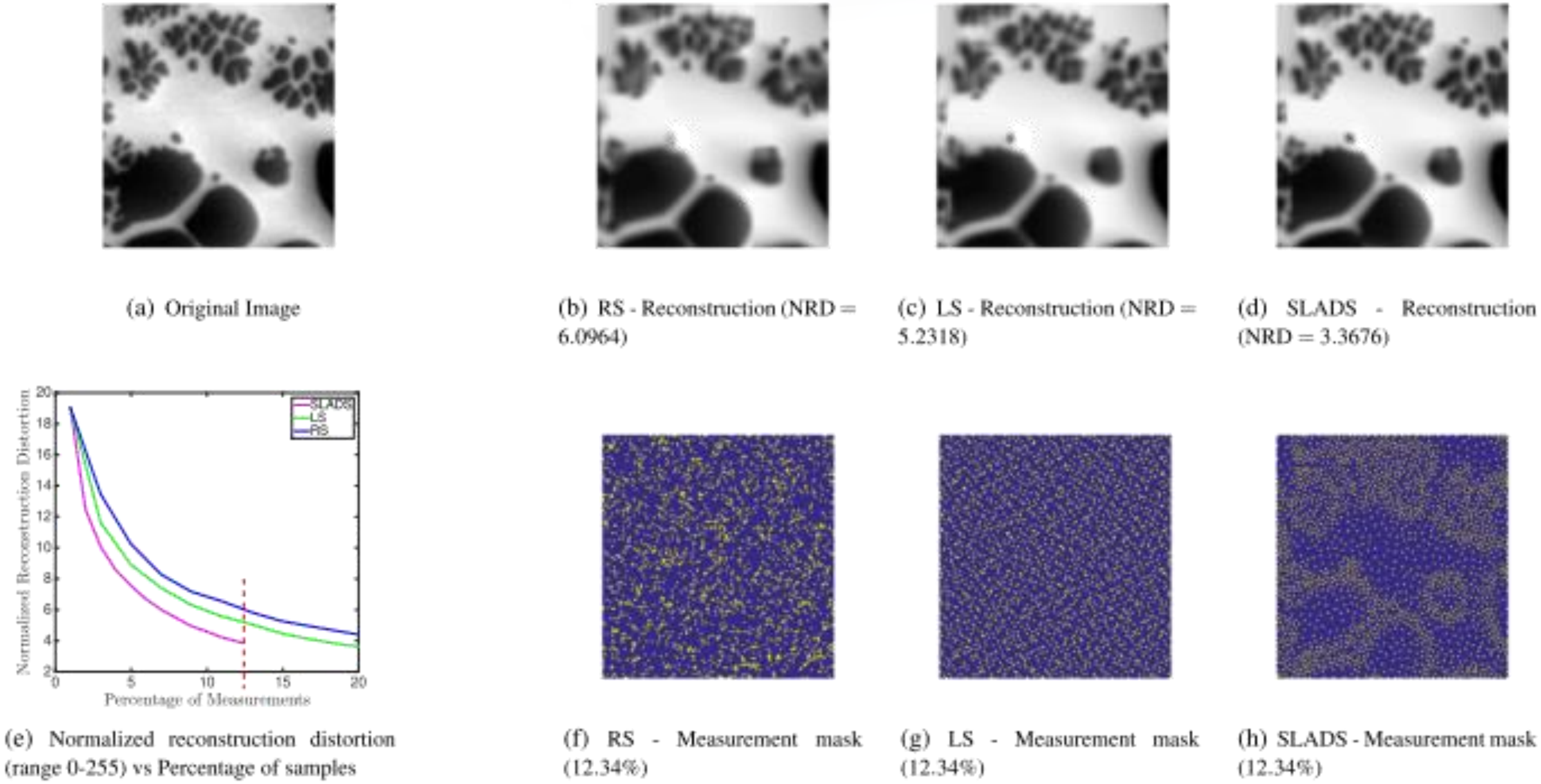


Figure 6. *Dynamic sampling results for SLADS compared with RS and LS for a continuously valued image. Here (a) is the image being sampled. (d) shows the image reconstructed from the samples prescribed by the SLADS algorithm. (b) and (c) show the images reconstructed using the same number of samples as SLADS but selected using from RS and LS respectively. (e) shows the normalized reconstruction distortion (NRD) versus the percentage of samples curves for the three methods. (f), (g) and (h) are the measurement masks that correspond to the reconstructions (b), (c) and (d) respectively.*

Some examples – 3/4

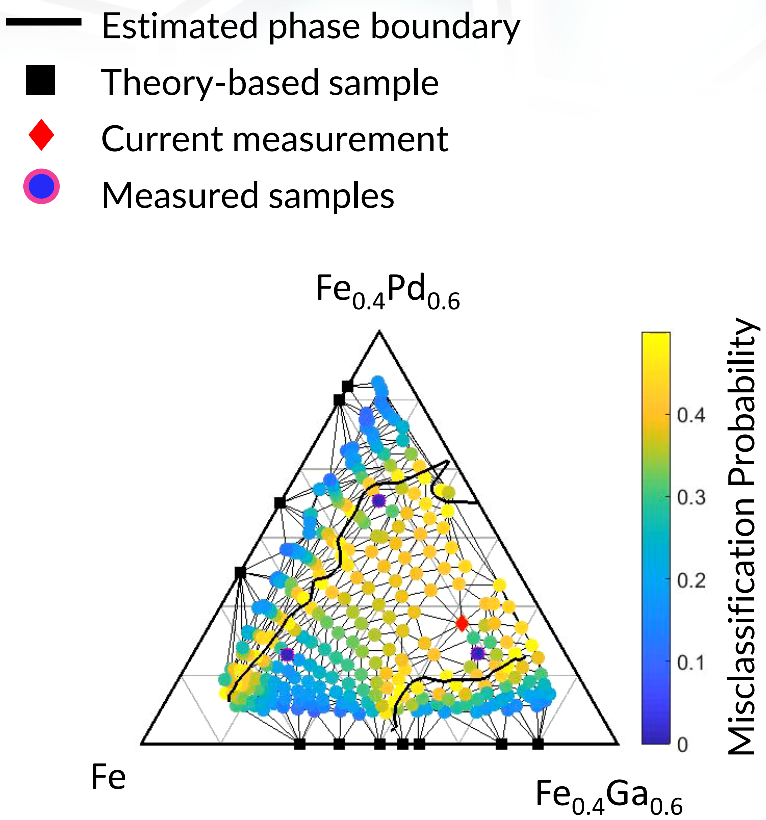
Gilad Kusne –
aaron.kusne@nist.gov

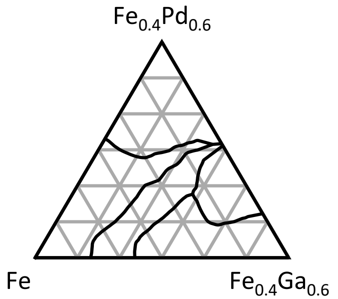
- **Autonomous metrology**

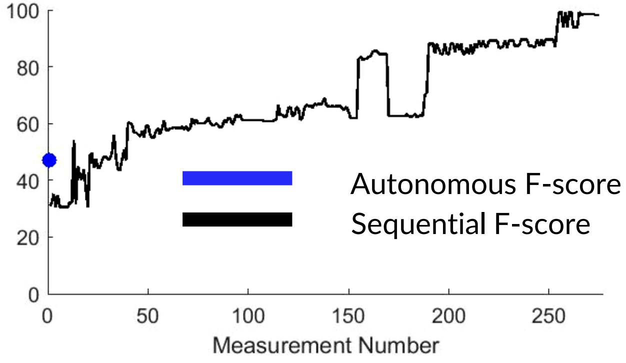
  A. Kusne, I. Takeuchi, *et al.*, *Nanotechnology*, 26, 444002, 2015

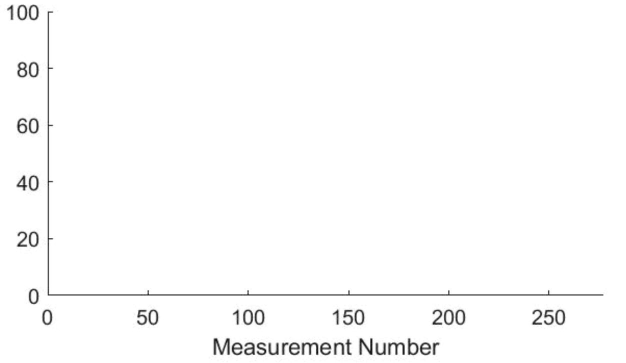
  …and recent unpublished results

- High-throughput XRD for combinatorial materials discovery
- Autonomous phase diagram mapping of composition spread wafer
- Phase diagram is estimated at each step based on collected data and physics-informed ML algorithms
- Unsupervised AI determines new composition to measure to best estimate phase diagram









AI is directly controlling the X-ray diffraction systems at SLAC

Some examples – 4/4

- **Compressive sensing**

  A. Stevens, N. Browning, *et al.*
  Microscopy, 63, 41-51, 2014.

- Intentionally acquire image at severe undersampling conditions
- Use ℓ_1-norm convex optimization to fill in the missing details
- An interesting means to get around the Nyquist-Shannon limit
- Demonstrated with random sampling in both STEM and SEM

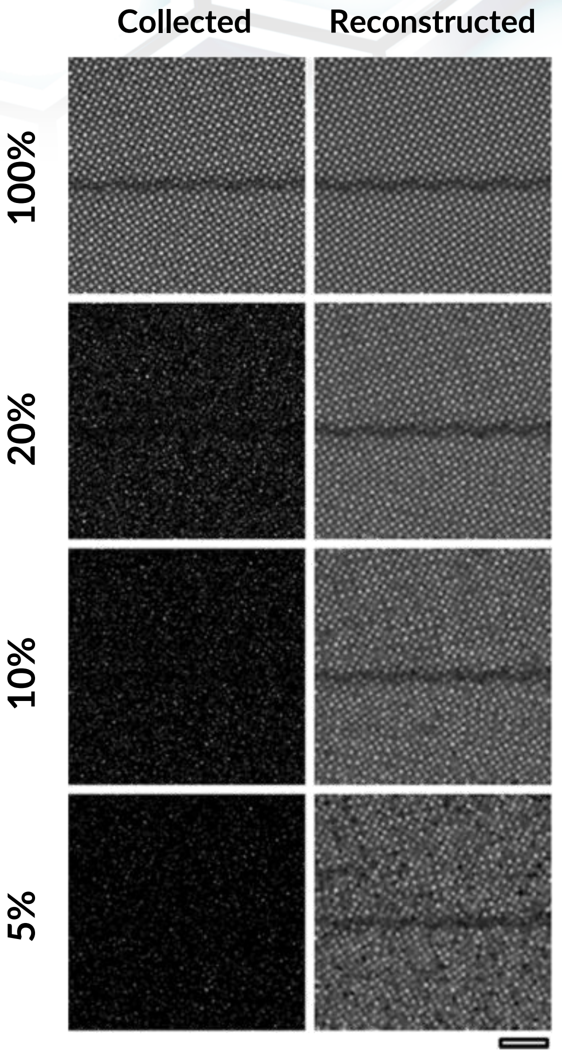


Fig. 7. Compressive reconstruction of the $SrTiO_3$ image. From top to bottom: 100, 20, 10 and 5% samples. The left column is the sampled image and the right column is the reconstructed image. Note that the 100% sample is only denoised. Scale bar, 2 nm.

$SrTiO_3$

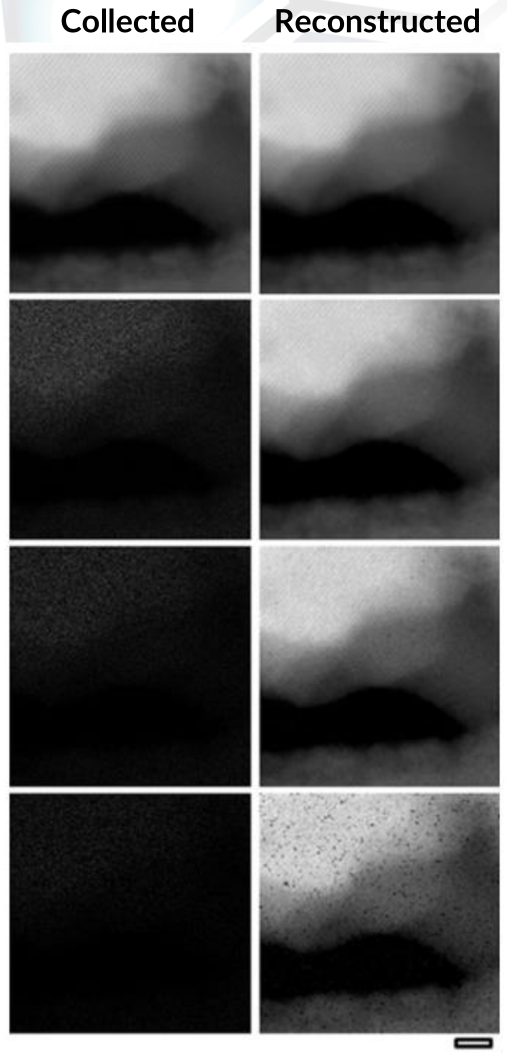


Fig. 11. Compressive reconstruction of zeolite image. From top to bottom: 100, 20, 10 and 5% samples. The left column is the sampled image and the right column is the reconstructed image. Note that the 100% sample is only denoised. Scale bar, 10 nm.

Zeolite

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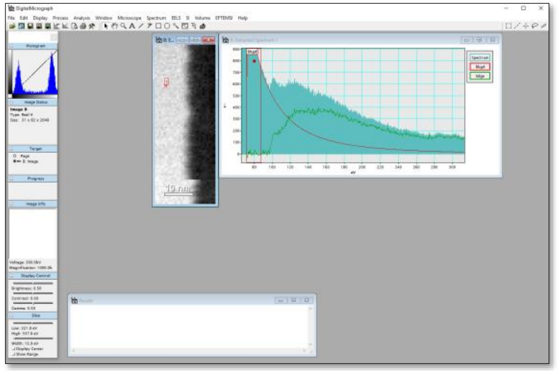
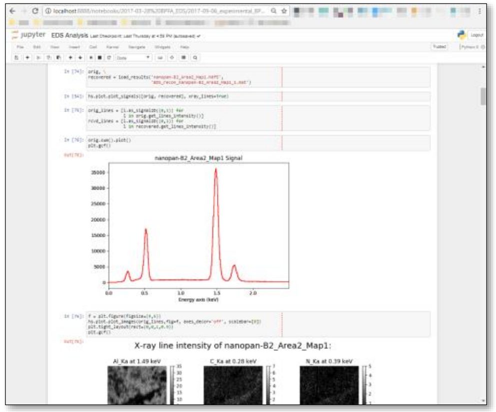
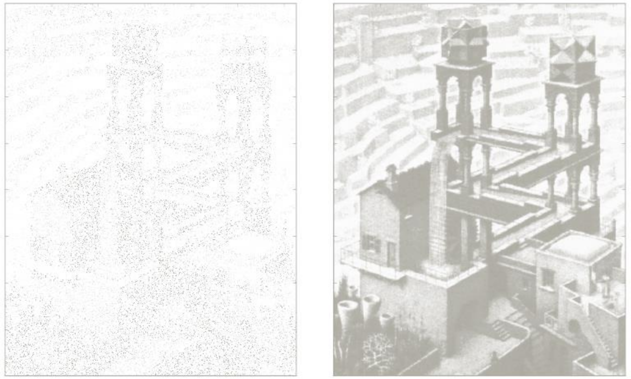
interactive GUI



Open/reproducible
notebook GUI



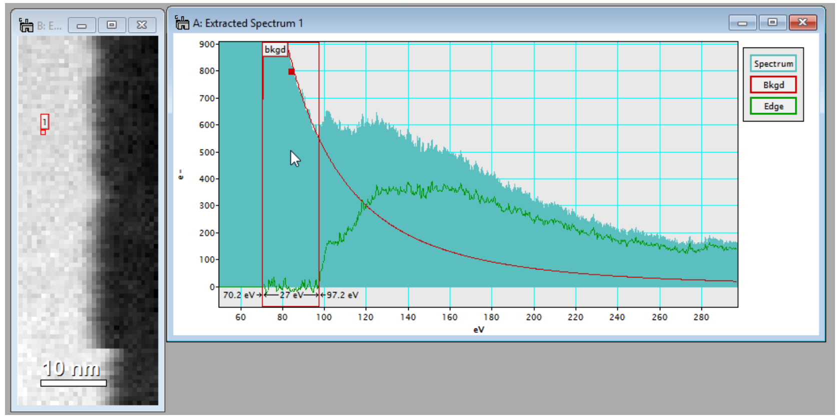
Compressed
Sensing

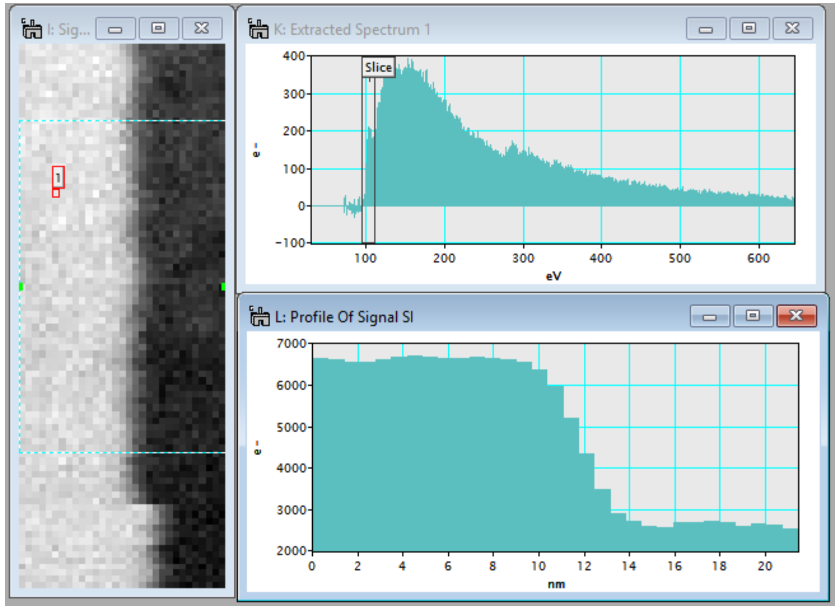


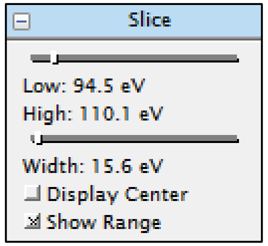
http://www.pyrunner.com

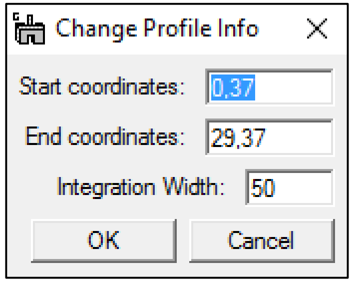
Moving towards reproducible microscopy

- **One or more software packages typically necessary**
- **Often vendor-provided**
- **GUI-driven with many options, sometimes “black-box”**
- **Typically, no log recorded**
  - Hope you keep a good notebook!
- **Tightly integrated with equipment/acquisition**



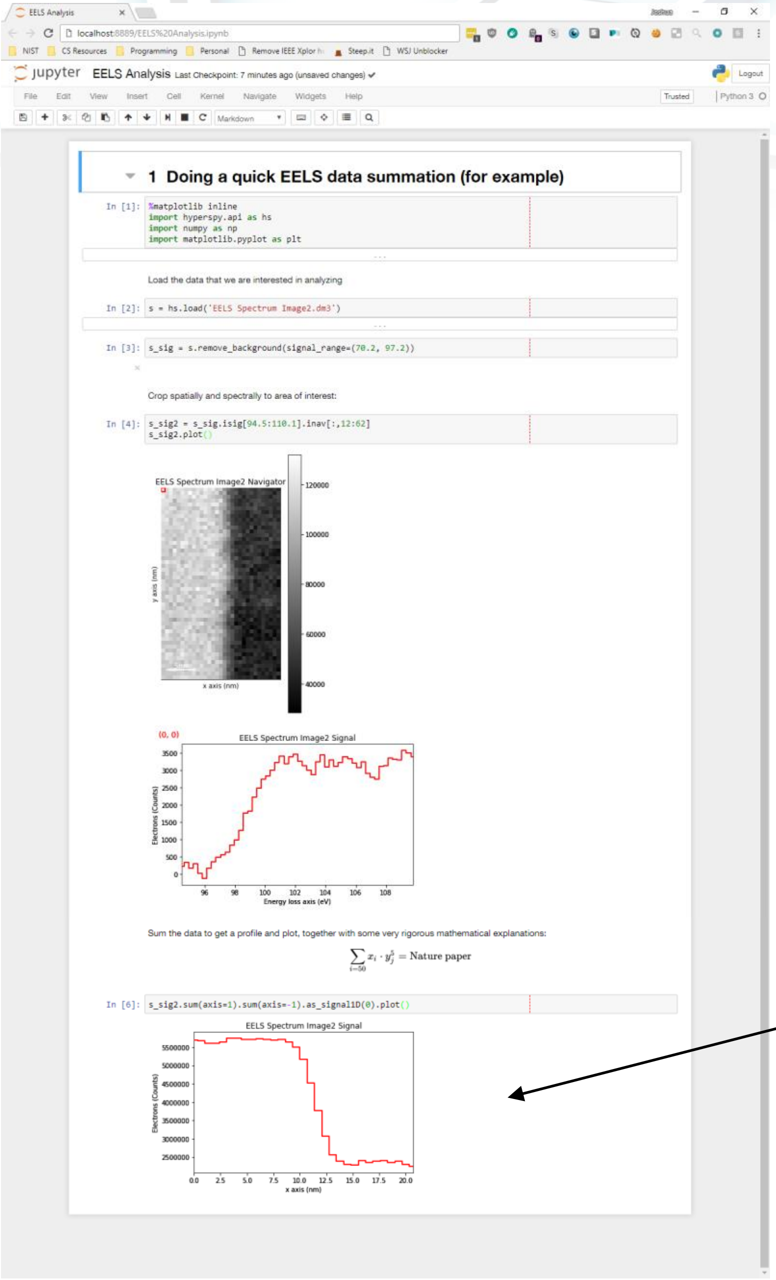


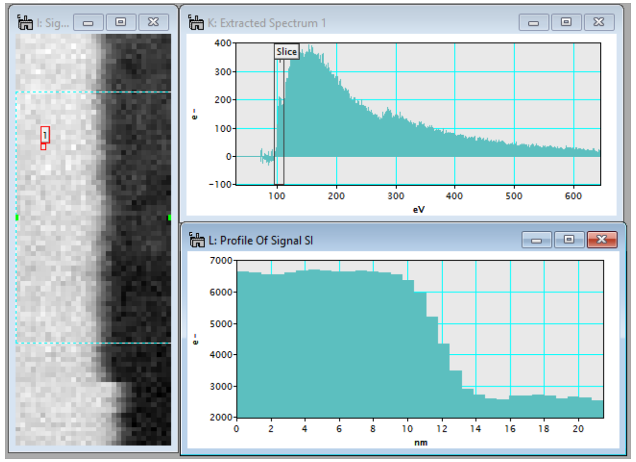




A better way…

- **Computation within a "notebook" environment**
- **Seamless mixing of notetaking, mathematics, and data analysis**
- **Notebook is rendered in any web browser**
- **Version controlled and exportable to PDF, HTML, Markdown, etc.**





Compare!

A better way…

- **Notebook-based tools are used extensively in data science**
  - Jupyter Notebook - http://jupyter.org/ is open-source option
    - Works with Python, Julia, R, Scala, Matlab, Fortran, Ruby, Spark, Go, C, etc.
    - With Python (and others): robust open-source 3rd-party libraries for many features
  - Proprietary options:
    - Mathematica, Maple

HyperSpy
multi-dimensional data analysis

- **Other options**
  - GUI recorders and reporting
  - Data pipelines – Common Workflow Language (CWL)
- **Requires data interoperability**

My “ideal” picture for research dissemination

- **Publishing should require workflow along with results**
  - Trying to reproduce others’ implementations is a waste of scientific (and financial) capital
  - A “journal article” should be able to be downloaded and the analysis reproduced
  - Like a supercharged “Methods” section

- **Does not need to be command line-based**
  - GUI tools that record interactions and options
  - Import/export states of execution
  - A common language would help

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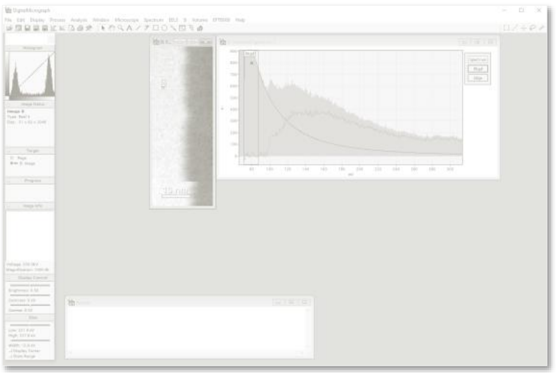
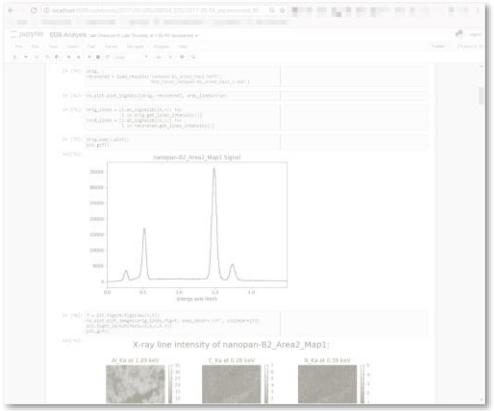
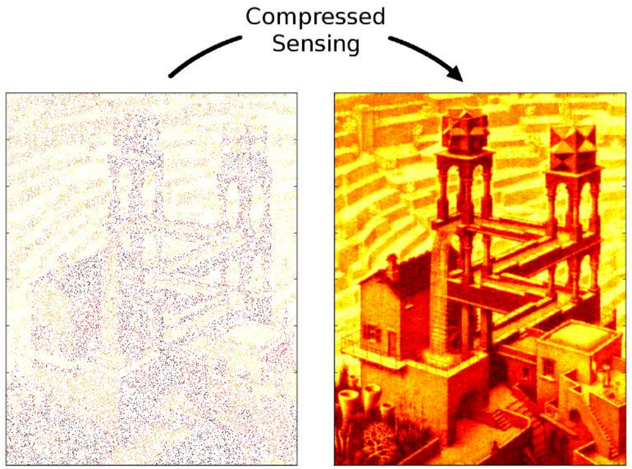
Proprietary/ interactive GUI



Open/reproducible notebook GUI

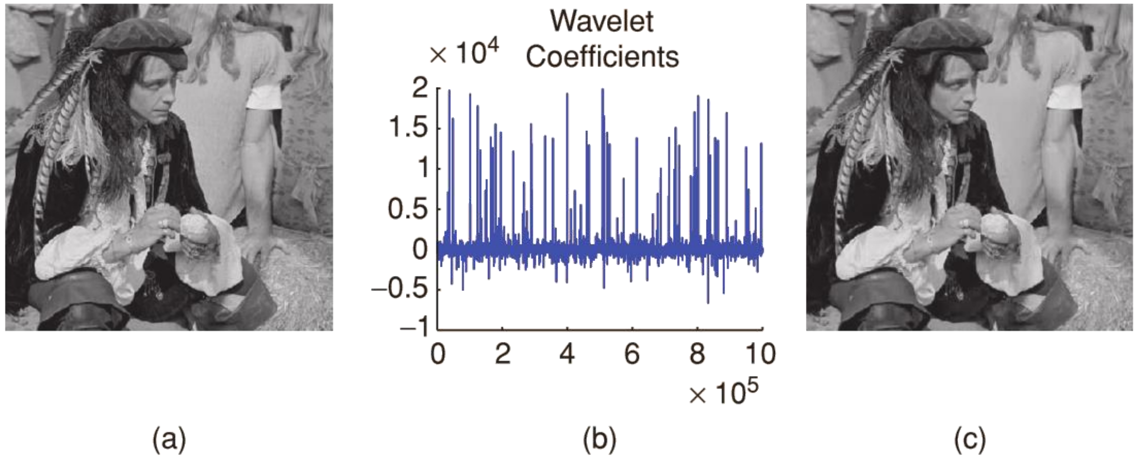




http://www.pyrunner.com

Motivation behind compressive sensing (CS)

- **Consider JPEG(2000) compression**
  - Acquire raw pixel values from camera sensor (large – many megapixels)
  - Decompose into wavelet basis
  - Discard small coefficients Store only “important coefficients” (small file size)
  - Decode image back into pixel basis for viewing
- **Why spend time acquiring data we just throw away?**



E.J. Candès and M.B. Wakin, *IEEE Signal Process. Mag*. 25, 21–30 (2008)

What is compressed sensing (CS)?

- **CS describes the perfect recovery of certain signals using a drastically reduced number of samples compared to Nyquist**
  - Traditional Nyquist limit says we need at least 2x highest frequency samples

- **Two conditions needed for successful CS:**
  - The **signal** must be **sparse** in some domain (basis)
  - The signal must be **sensed** in an **incoherent** manner

More reading for good introductions to the theory:

- E.J. Candès and M.B. Wakin, An Introduction To Compressive Sampling, *IEEE Signal Process. Mag*. **25**, 21 (2008).
- K. Bryan and T. Leise, Making Do with Less: An Introduction to Compressed Sensing, *SIAM Rev*. **55**, 547 (2013).

What is compressed sensing (CS)?

- **Two conditions needed for successful CS:**

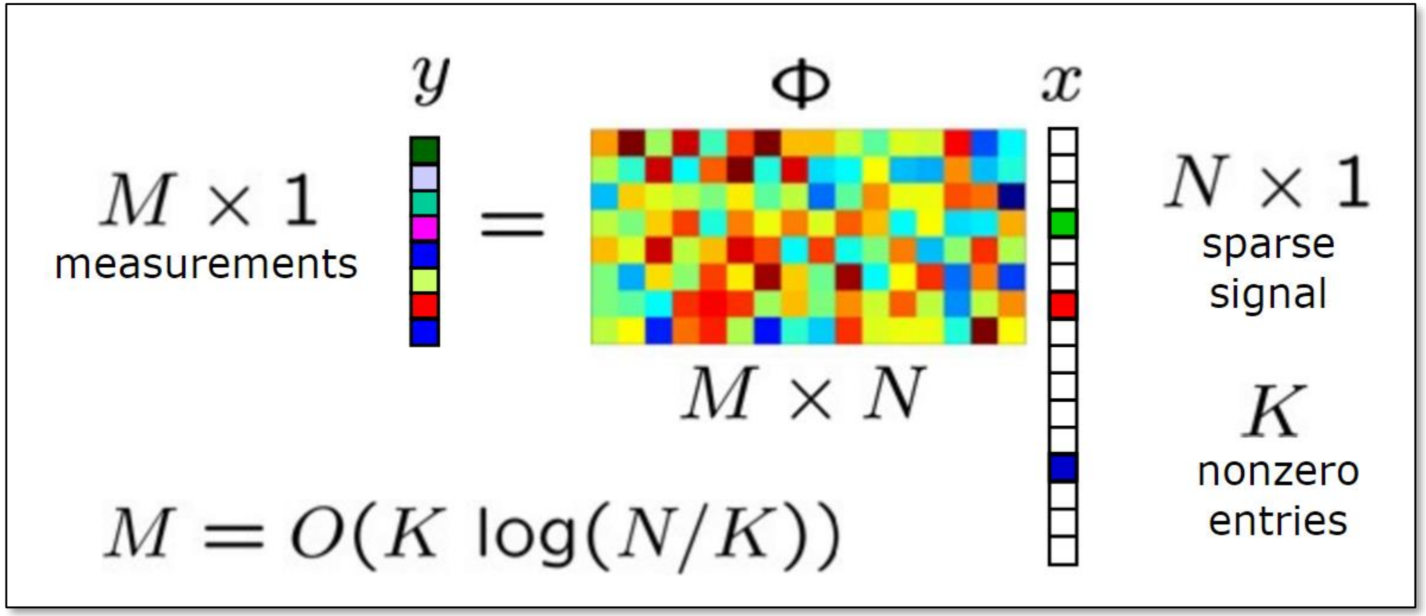
  - The **signal** must be **sparse** in some domain (basis)
    - Sparsity ≈ compressibility – we know natural images can be represented sparsely
    - If your image (or spectrum image) can be highly compressed, it is likely sparse!

  - The signal must be **sensed** in an **incoherent** manner
    - An entire lecture could be devoted to incoherence
    - For practical applications, uniform random sampling satisfies the incoherence necessity

Slightly more technical description

- **Consider an unknown signal to be measured x**
- **$\boldsymbol{\Phi}$ is the known "sensing" or measurement matrix**
- **y is our known measurement vector**

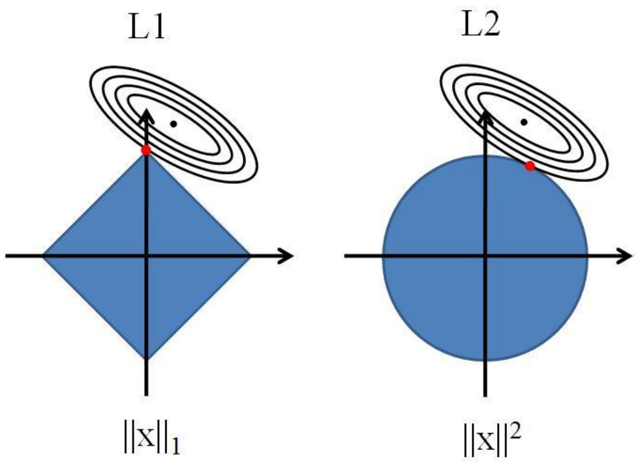
- **We need to solve for x, given $y = \boldsymbol{\Phi} x$**



Richard Baraniuk

Slightly more technical description

- **Φ has fewer rows than columns, so $y = \Phi x$ is underdetermined**
  - This means there are an infinite number of solutions
- **The "magic" of compressed sensing is the use of the ℓ_1 norm for convex optimization to find the "best" $\mathbf{x}$ (when using the right Φ)**

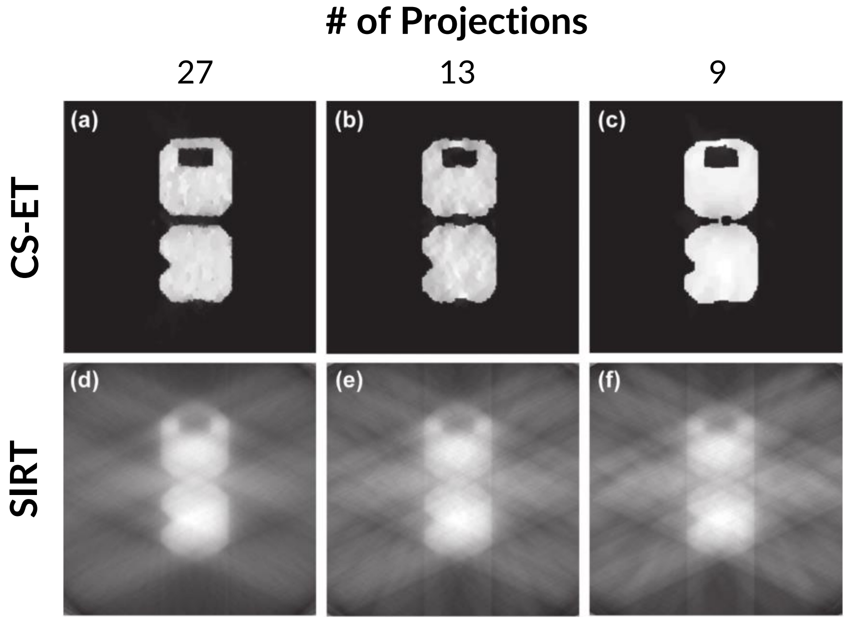


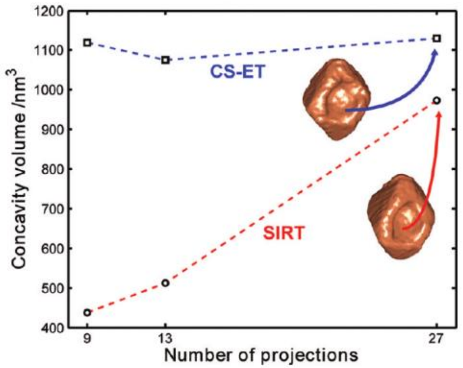
T. Zhou. "Compressed Sensing Review (1): Reconstruction Algorithms." *Tianyi Zhou's Research Blog*, (2010).

	Minimizing Norm	Definition	Description
NP-hard! →	ℓ_0	$\|x\|_0 = \sqrt[0]{\Sigma_i x_i^0} = \#(i\|x_i \neq 0)$	Number of non-zero components
	ℓ_1	$\|x\|_1 = \Sigma_i \|x_i\|$	*Manhattan* distance (Sum of Absolute Difference)
Bad results →	ℓ_2	$\|x\|_2 = \sqrt{\Sigma_i x_i^2}$	Euclidean distance (Least squares difference)

CS in TEM (electron tomography – CS-ET)

- **Tilt-tomography finds 3D representations of objects in the TEM by acquiring 2D images at many tilt angles**
  - Can reduce number of tilted images needed using CS principles and compare results to the standard *simultaneous iterative reconstruction technique* (SIRT)
- **Tomography of iron oxide nanoparticles:**
  - CS-ET performs significantly better than SIRT, at all signal levels



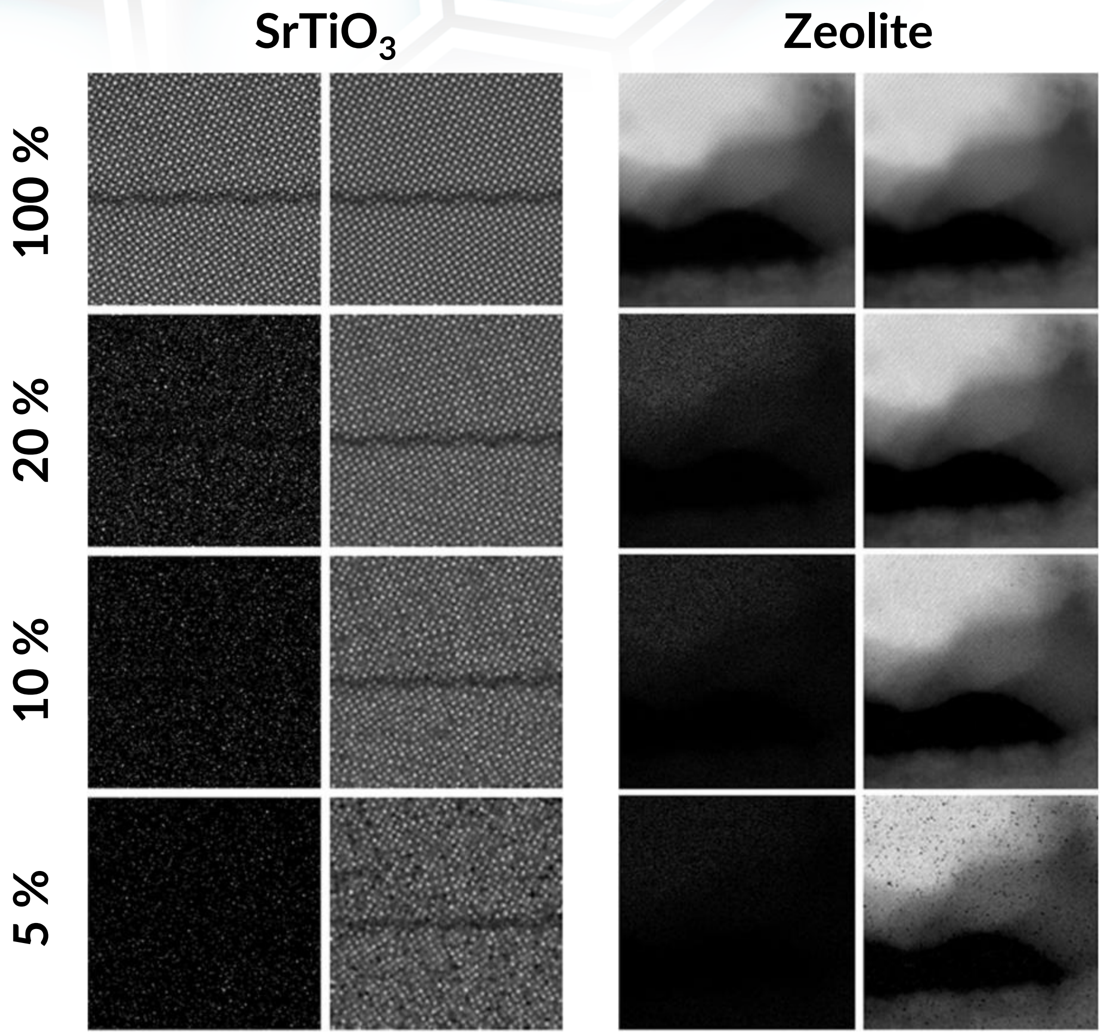


Z. Saghi, *et al.* Three-dimensional morphology of iron oxide nanoparticles with reactive concave surfaces. A compressed sensing-electron tomography (CS-ET) approach, *Nano Lett*. **11**, 4666 (2011).

R.K. Leary, *et al.*, Compressed sensing electron tomography, *Ultramicroscopy*. **131**, 70 (2013).

CS in STEM (imaging)

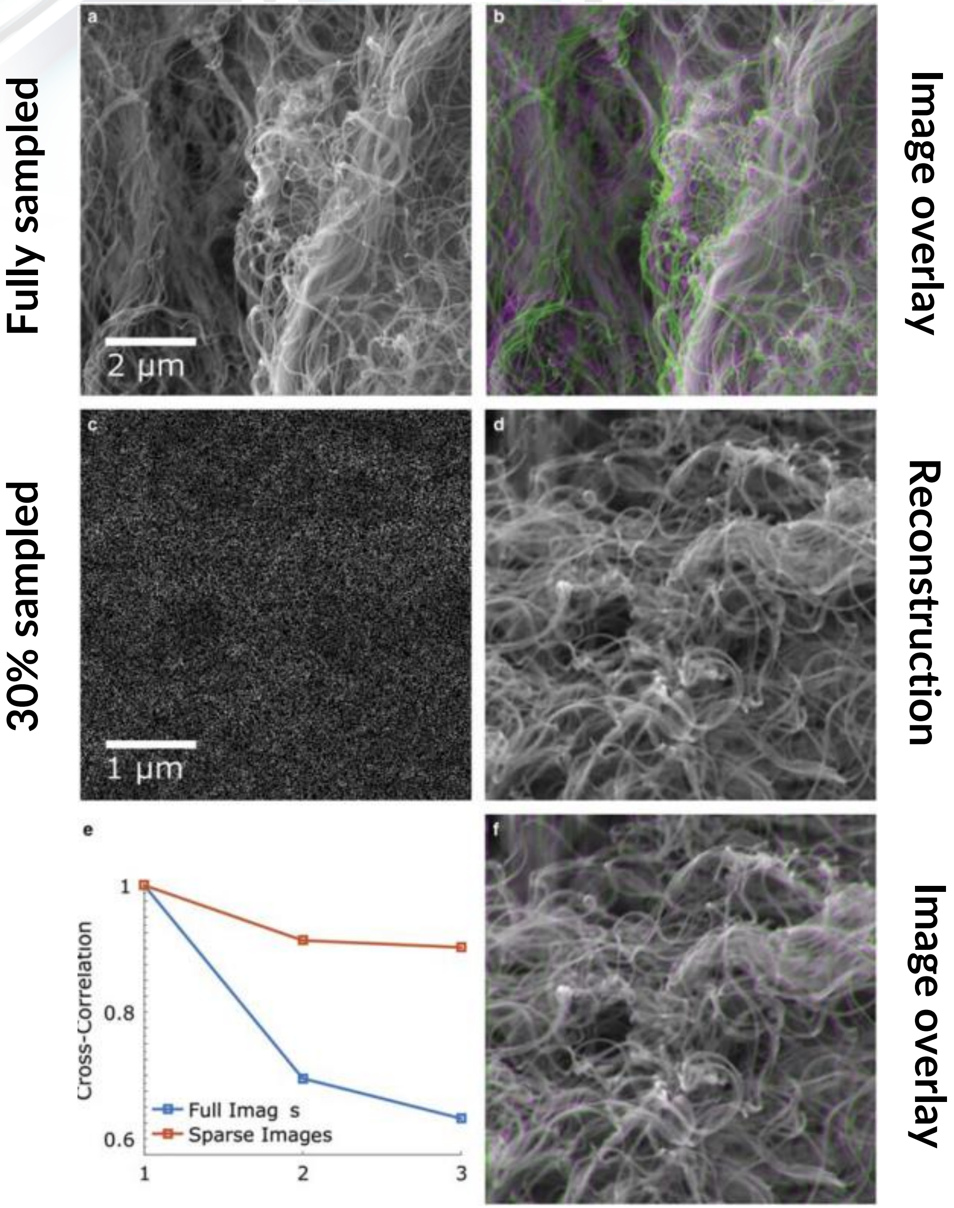
- **Benefits of reduced sampling in STEM:**
  - Reduced dose (for electron-sensitive materials)
  - Reduced time/increased throughput
- **Random sampling in pixel-domain**
  - Bayesian factor analysis to find sparse representation (BPFA)
  - Sampling done with beam blanker or meandering beam



A. Stevens, *et al.*, The potential for Bayesian compressive sensing to significantly reduce electron dose in high-resolution STEM images, Microscopy. 63, 41 (2014).

CS in SEM

- K. Hujsak, *et al.*, Suppressing Electron Exposure Artifacts: An Electron Scanning Paradigm with Bayesian Machine Learning, Microscopy and Microanalysis, 1–11 (2016).
  - Analyzed effect of reduced dose from CS-SEM on electron-sensitive human collagen sample
  - Significant reduction in sample modification due to beam-damage
- Also tested various scan patterns
  - Random sampling was found to perform better than spiral, Lissajous, and random line sampling
  - Highest reconstructed PSNR and least number of scanning artifacts



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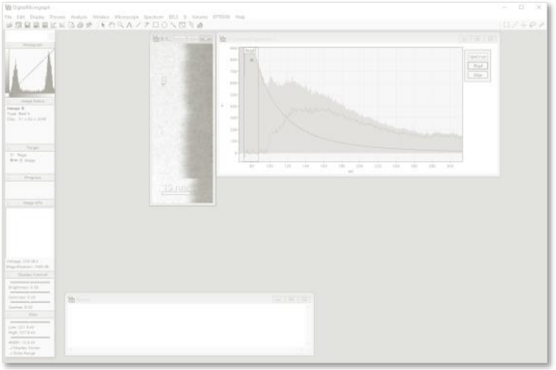

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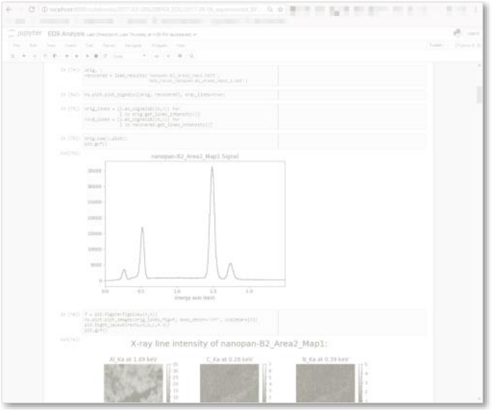
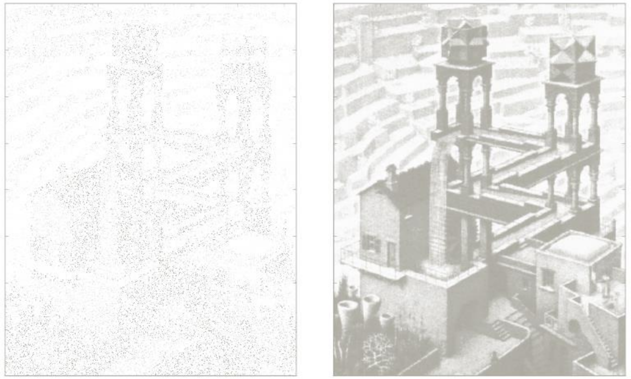


Compressed Sensing

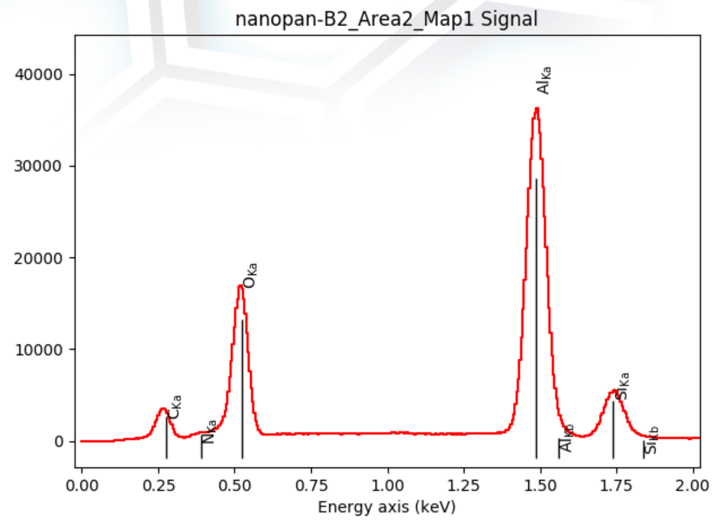


http://www.pyrunner.com

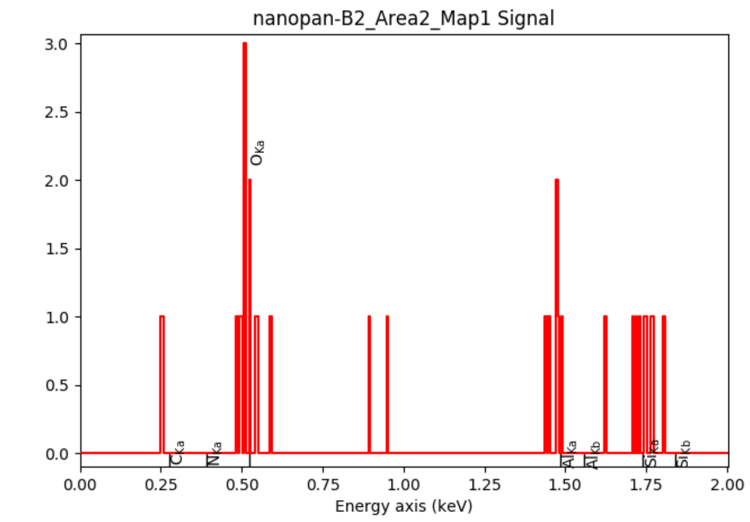
Our goals

- **Exploring CS applications in the microanalytical realm**

- **EDS in the FIB-SEM can take a very long time (especially in 3D)**
    - Long dwell times needed
    - 2D maps are very often sparse in a pixel basis
    - Acquisitions will damage beam-sensitive materials



Summed area spectrum



Individual pixel spectrum

BPFA = Beta-Bernoulli Process Factor Analysis

- **Factor analysis**
  - Decompose signal into a linear approximation of factors and weights

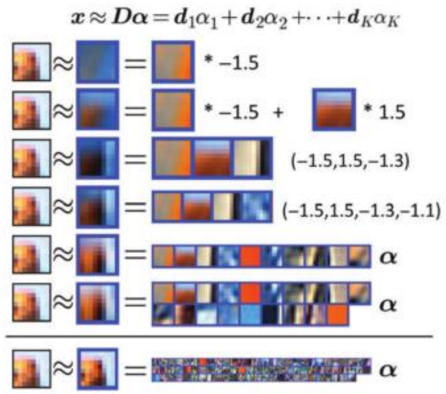
$$\boldsymbol{x}_i = \mathbf{D}\,\boldsymbol{w}_i + \boldsymbol{\epsilon}_i$$

Noise and residual

Original data samples

Dictionary matrix of “prototypical” signals

Dictionary element weights (vector)



An image patch ($\boldsymbol{x}_i$) can be represented by a dictionary ($\mathbf{D}$) of representative patches, with each element weighted by a factor from $\boldsymbol{w}$ (plus some noise $\boldsymbol{\epsilon}$)

Figure from: A. Stevens, et al. *Microscopy*. **63**, 41 (2014).
Note: $w_i = \alpha_i$ *in this paper’s notation*

BPFA = Beta-Bernoulli Process Factor Analysis

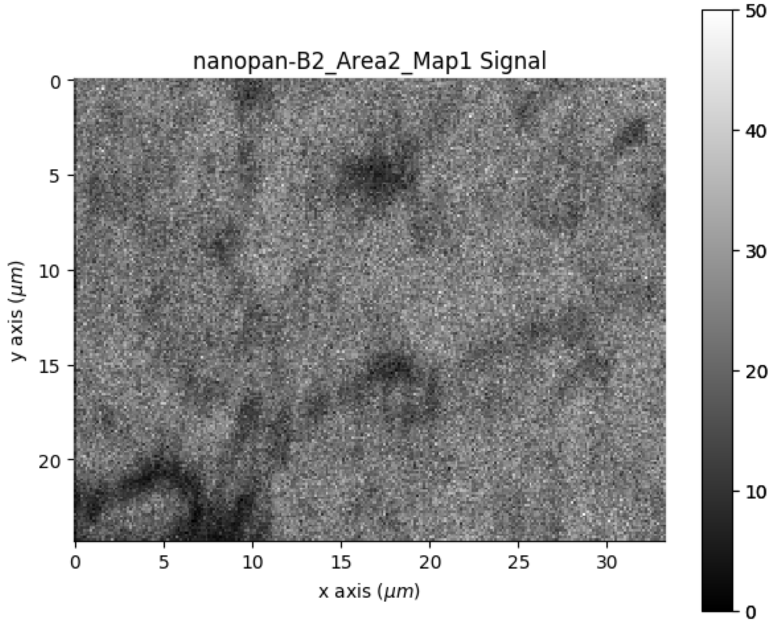
- **How to find $\mathbf{D}$ and $\boldsymbol{w}$?**
  - Bayesian beta-Bernoulli Process
- **We infer the underlying signal $\boldsymbol{x}_i = \mathbf{D}\boldsymbol{w}_i$ by:**
  - Placing Bayesian priors on $\mathbf{D}$, $\boldsymbol{w}_i$, and $\boldsymbol{\epsilon}_i$
  - Assuming that $\boldsymbol{w}_i$ is sparse
  - Iterate to obtain approximation of $\boldsymbol{x}$ using a sparse representation from the elements of $\mathbf{D}$

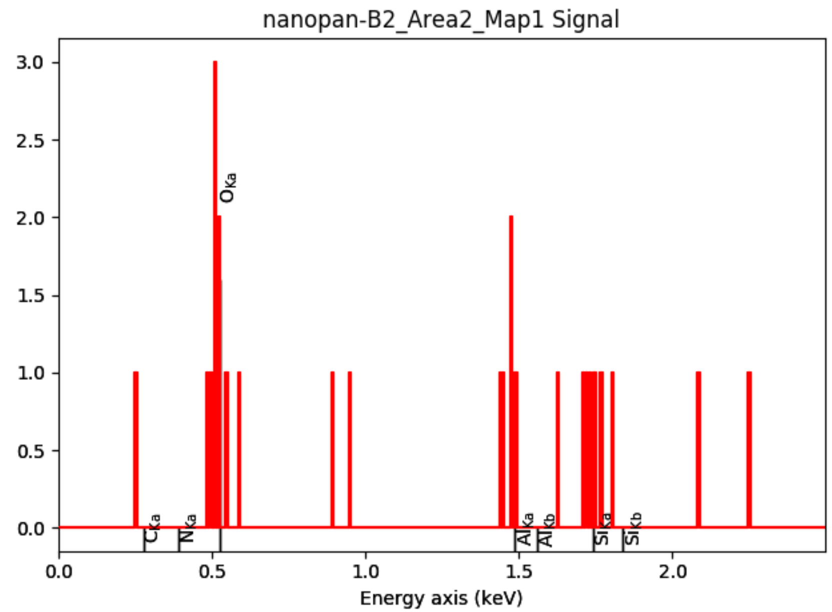
Details about algorithms in:

- M. Zhou, et al., Nonparametric bayesian dictionary learning for analysis of noisy and incomplete images, *IEEE Trans. Image Process*. **21**, 130–144 (2012)
- Z. Xing, et al., Dictionary Learning for Noisy and Incomplete Hyperspectral Images, *SIAM J. Imaging Sci*. **5**, 33–56 (2012).

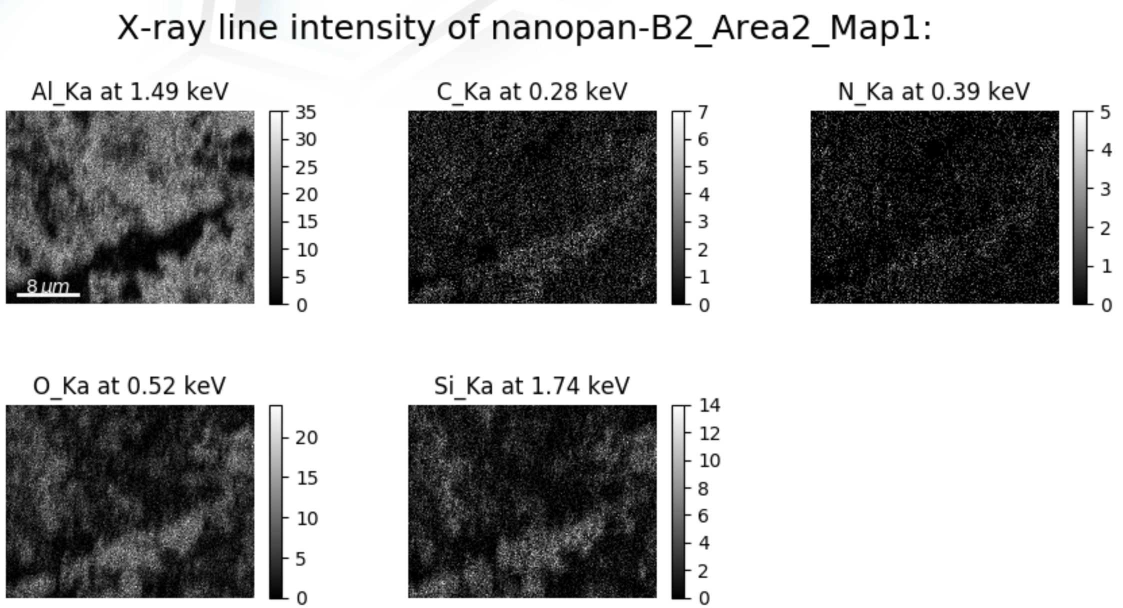
What does it look like in practice?

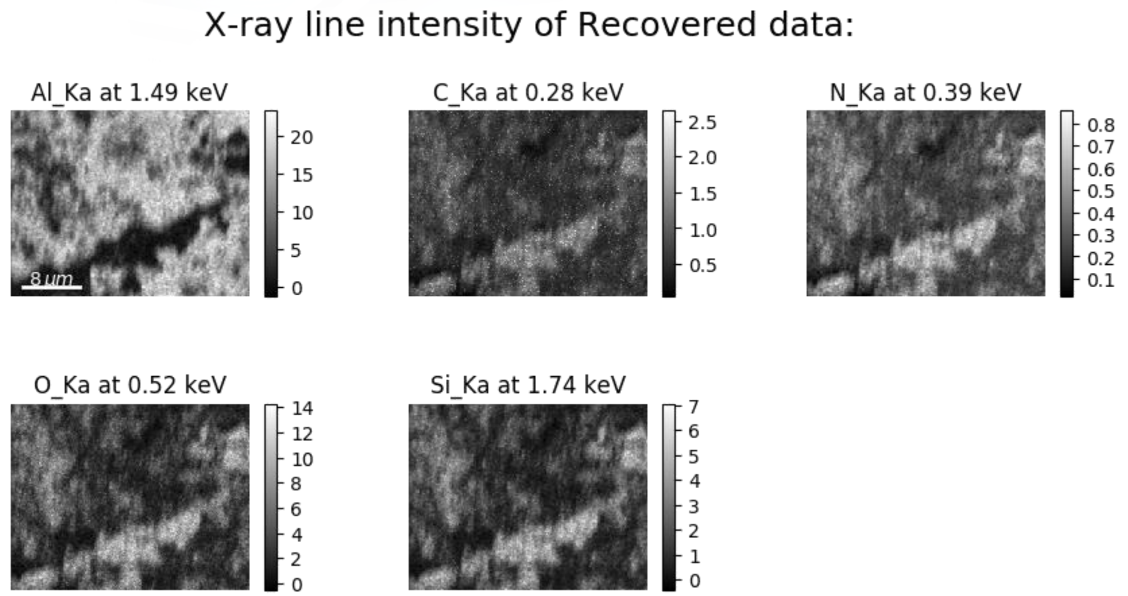
- **Example EDS maps**
  - ~ 256 x 200 pixels
  - 5, 10, and 15 kV V_{acc}
  - Analyzing nano-scale precipitates in aluminum silicates



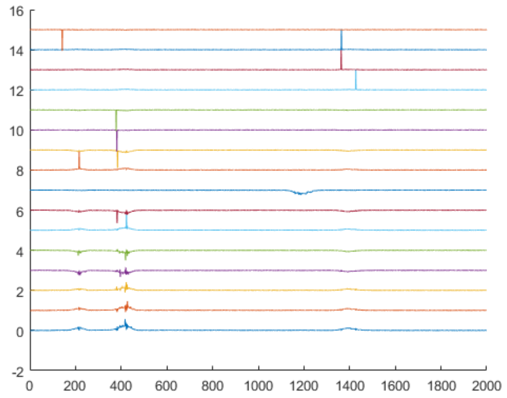


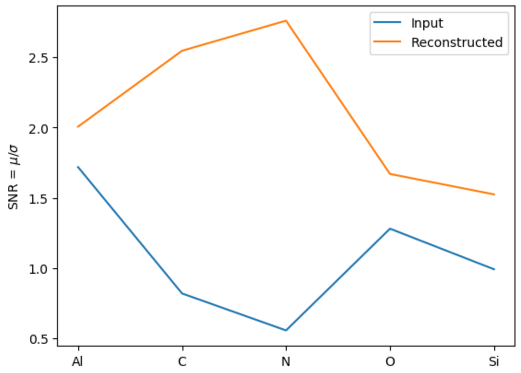
BPFA on sparse EDS maps



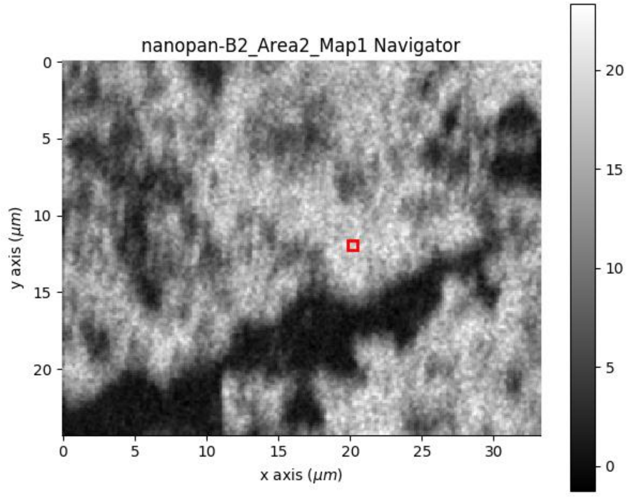


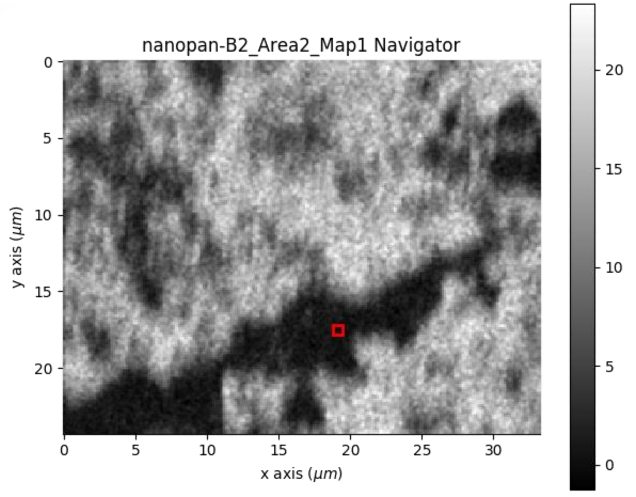
- **BPFA successfully reconstructs the EDS data**
  - Dictionary of 16 “spectra”
  - Signal to noise improvement
- **Artifacts**
  - Spikes in dictionary elements
  - May need longer to fully converge

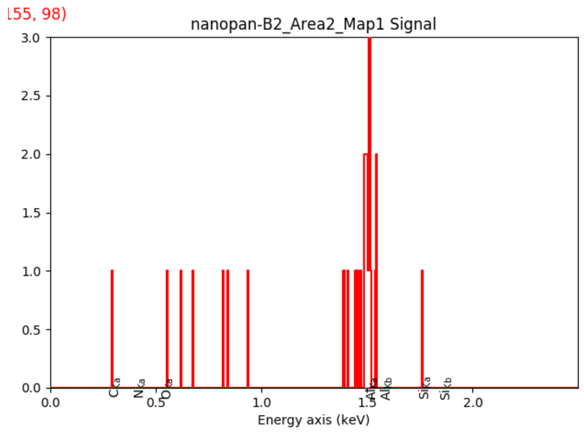


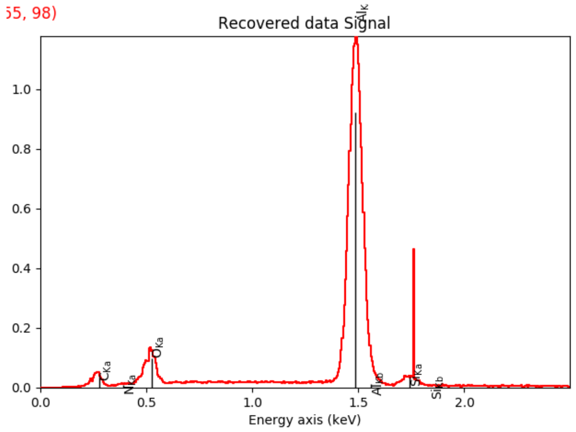


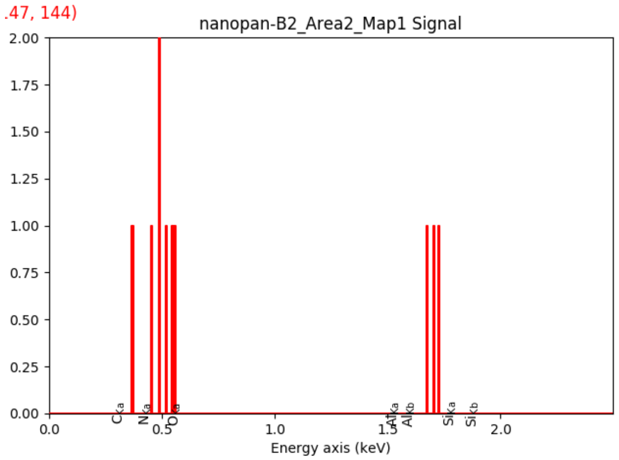
BPFA on sparse EDS maps

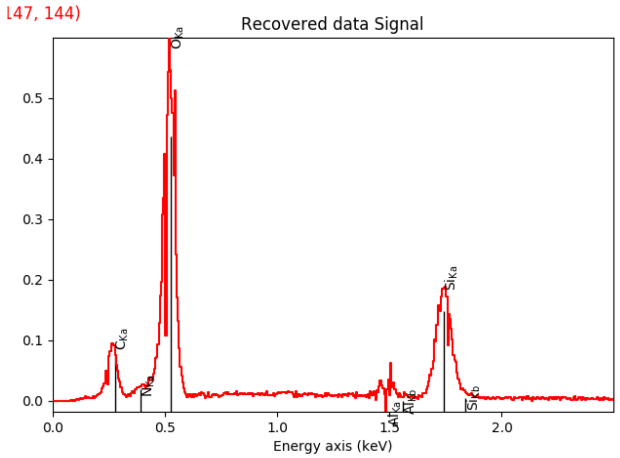




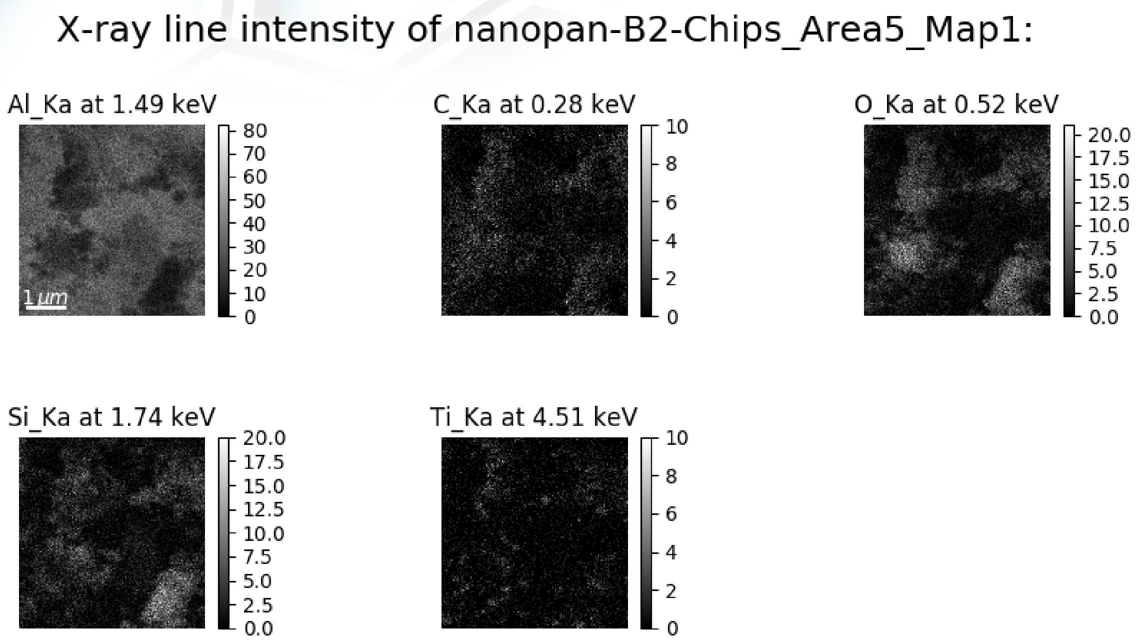


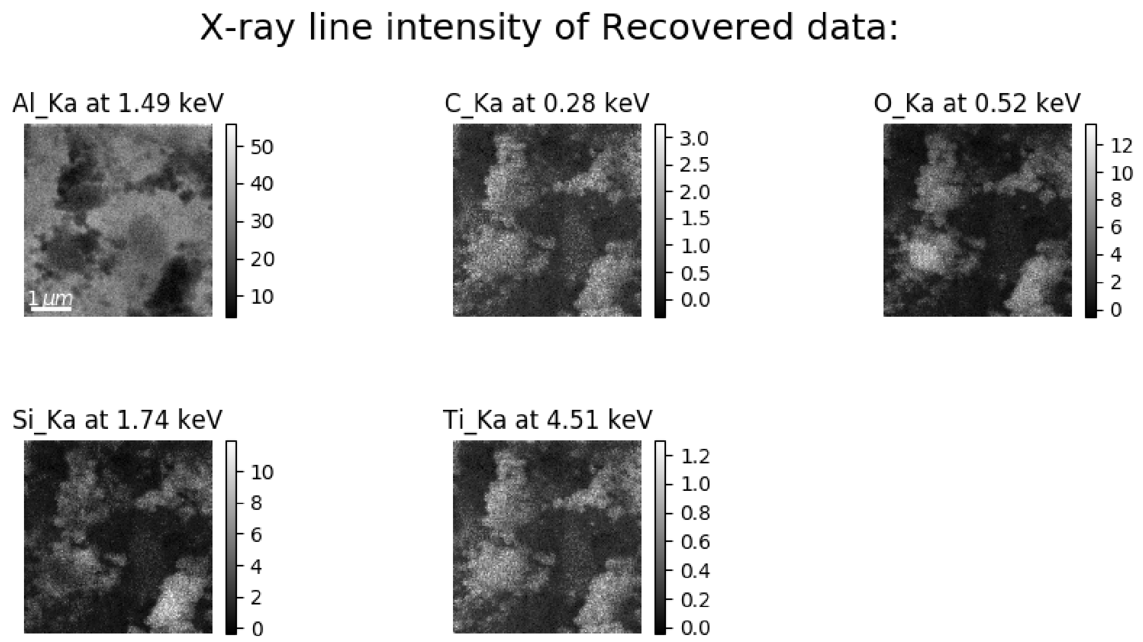




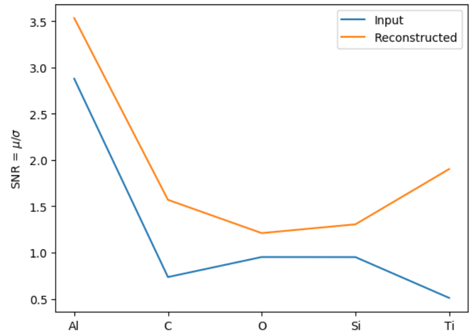


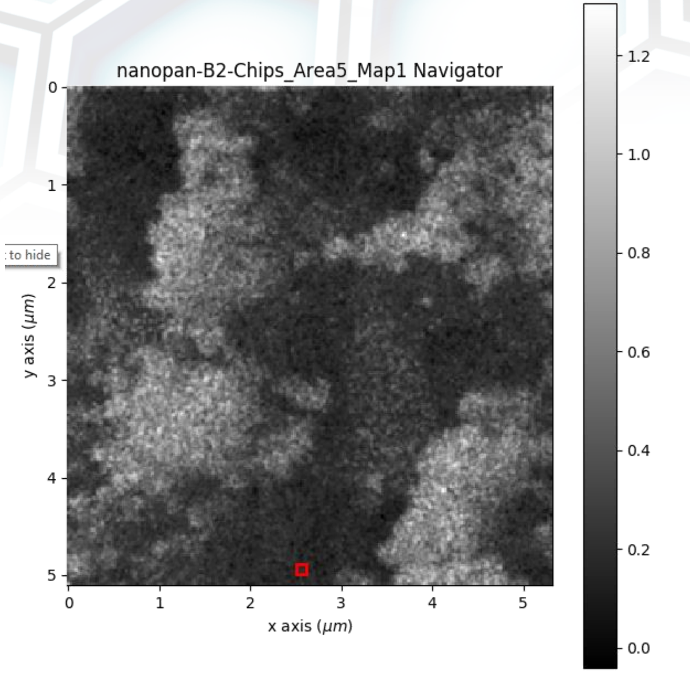
BPFA on more sparse EDS maps

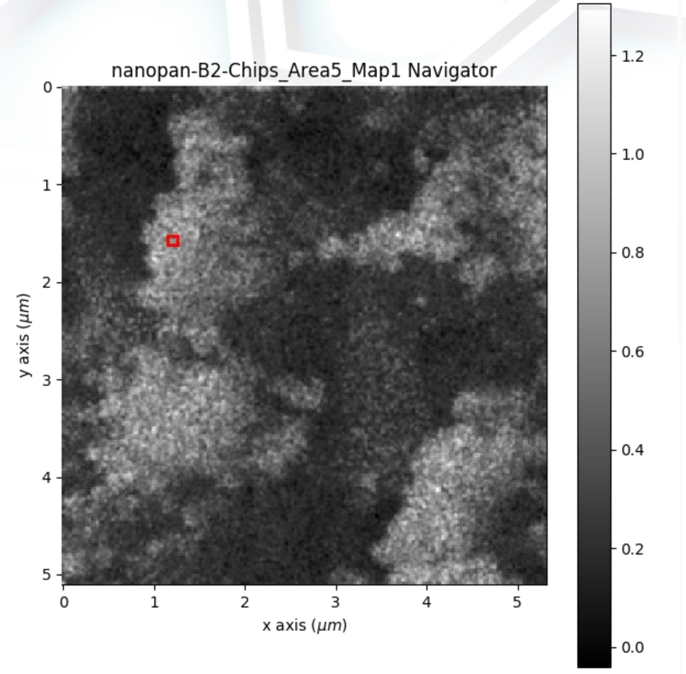


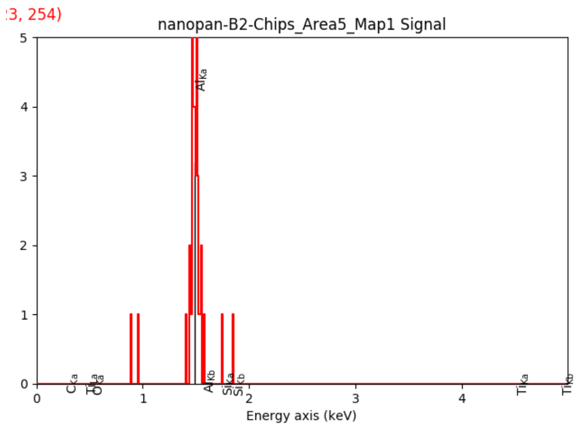


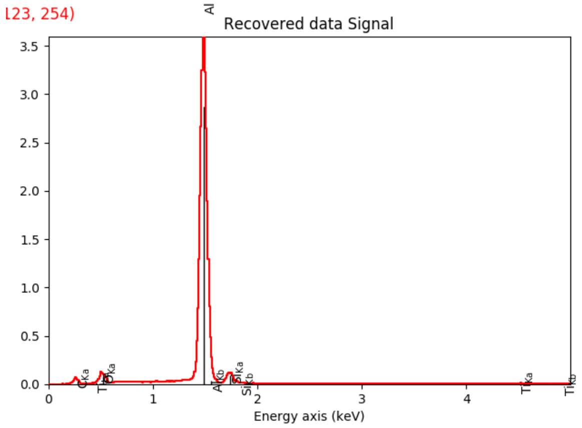
- **Again, successful reconstruction**
- **Significant contrast enhancement in all line images**
  - Is enhancement of Ti a real effect, or artifact?

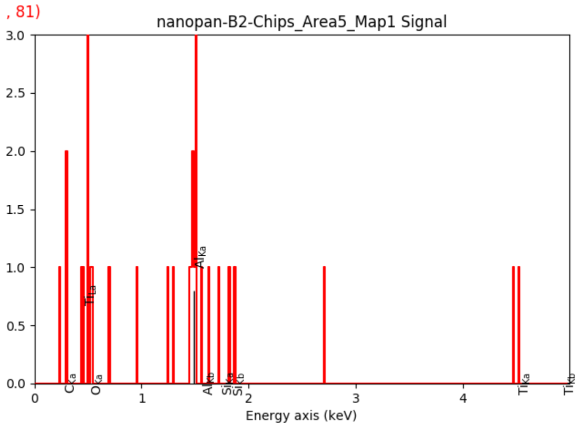


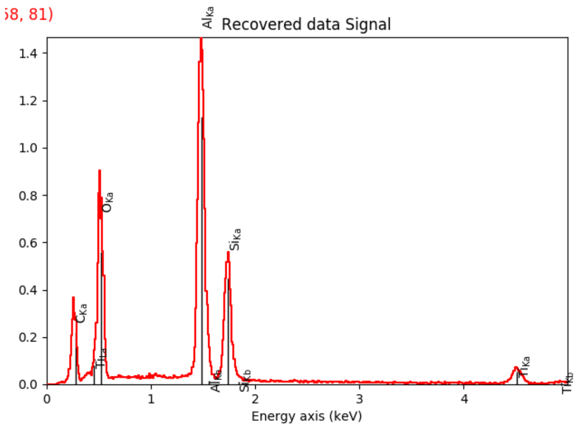

nanopan-B2-Chips_Area5_Map1 Navigator
y axis (μm)
x axis (μm)
to hide


nanopan-B2-Chips_Area5_Map1 Navigator
y axis (μm)
x axis (μm)


3, 254)
nanopan-B2-Chips_Area5_Map1 Signal
Energy axis (keV)


123, 254)
Recovered data Signal
Energy axis (keV)


, 81)
nanopan-B2-Chips_Area5_Map1 Signal
Energy axis (keV)


58, 81)
Recovered data Signal
Energy axis (keV)

Promising results, but lots more work to be done

- **Comparison of reconstructions to "ground truth" acquisitions**
  - i.e. how do reconstructions compare to maps acquired with longer dwells?
- **Investigating impacts on quantification, component analysis, phase mapping, etc.**
- **Expansion to three dimensions**
  - Should be able to go even sparser in each 2D map by incorporating information from adjacent slices
- **Can these reconstructions be done in real-time?**
  - Optimization needed for practical on-tool use

Conclusions and Parting Thoughts

Computational microscopy is coming!

- **With ever-growing data sizes and improving computational resources, we are at the very beginning of this field**

- **These methods are very powerful, but their implications and validity are still not well understood**
    - Uncertainties, artefacts, etc.

- **Machines will soon be better at this than we are**
    - Better to make sure you're on the same team as them ☺

Thank you!

And Happy Birthday Dale!

Questions/comments?

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