 Imaging with electrons, in particular using scanning transmission electron microscopy (STEM), will become increasingly important in the near future, especially in the materials and life sciences. Understanding cellular interaction networks will enable transformative research such as “visual proteomics,” where spatial arrangements of the proteome or particular subsets of proteins will be mapped out. In the area of heterogeneous catalysis, which in many cases relies on nanoparticles deposited onto supports recently, achieved advances in imaging and characterization of catalysts and precatalysts are transforming the field and allowing more and more rational design of multifunctional catalysts. Advances in nanoscale manufacturing will require picometer resolution and control as well as the elimination of routine visual inspection by humans to become viable and implemented in “real” manufacturing environments. There are (at least) two major obstructions to fully exploit the information provided by electron microscopy.

On the one hand, a major bottleneck in all these applications is currently the “human-in-the-loop” resulting in slow and labor-intensive selection and accumulation of images. A “smart” microscope in which instrument control, image prescreening, image recognition, and machine learning techniques are integrated would transform the use of electron imaging in materials science, biology, and other fields of research by combining fast and reliable imaging with automated high-throughput analysis such as combinatorial chemical synthesis in catalysis or the multiple “omics” in biology.

On the other hand, even if environmental perturbations could be completely avoided a principal dilemma remains that results from the fact that the acquired images offer only an “ambiguous reflection” of reality due to inherently noisy data and this is the primary issue addressed in this volume. The noise structure is highly complex and far from fully being understood. In particular, it depends in a complex way on the electron dose deployed per unit area. Low noise levels require a high dose that, in turn, may cause damage. In most cases, high-energy electrons damage biological and organic matter and thus require special techniques for imaging when using electron microscopes with beams in the 100–300 kV range. Experiments are frequently performed at “nonbiological” temperatures

(i.e., cryo-electron microscopy) to reduce damage. But even when investigating inorganic material at the atomic resolution level, relatively low dose image acquisition is often required to avoid damaging the sample. This again impacts significantly the signal-to-noise ratio of the resulting images. The required low doses necessitate new paradigms for imaging, more sophisticated data “denoising” and image analysis as well as simulation techniques. In combination with ongoing experimental work to reduce the environmental impact during nano-imaging experiments (e.g., vibrations, temperature, acoustic, and electromagnetic interference), we have begun to develop and apply nonlinear probabilistic techniques. They are enhanced by learning theory to significantly reduce noise by systematically exploiting repetitive similarities of patterns within each frame as well as across a series of frames combined with new registration techniques. Equating “low electron dose” with “few measurements” is an intriguing idea that is going to radically alter image analysis—and even acquisition—using techniques derived from “Compressed Sensing,” an emerging new paradigm in signal processing. A key component here is to use randomness to extract the essential information from signals with “sparse information content” by reducing the number of measurements in ranges where the signal is sparse. Working first with inorganic materials allows us to validate our methods by selecting on the basis of high-resolution images an object to be imaged at lower resolution. Building on the insight gained through these we can then proceed to image silicate or organic materials which cannot be exposed to high energy electrons for extended periods of time. Examples of such an approach are given in Chap. 4.

Part of our work has greatly benefitted from three workshops organized at the University of South Carolina by the Interdisciplinary Mathematics Institute and the NanoCenter entitled “Imaging in Electron Microscopy” in 2009 and 2010 and “New Frontiers in Imaging and Sensing” in 2011. At these workshops world-class practitioners of electron microscopy, engineers, and mathematicians began to discuss and initiate innovative strategies for image analysis in electron microscopy.

The goal of our work is to develop and apply novel methods from signal and image processing, harmonic analysis, approximation theory, numerical analysis, and learning theory. Simulation is an important and necessary component of electron image analysis in order to assess errors of extracted structural parameters and better understand the specimen–electron interactions. It thereby helps improve the image as well as calibrate and assess the electron optics and their deviations due to environmental effects such as acoustic noise, temperature drifts, radio-frequency interferences, and stray AC and DC magnetic fields. The intuition-based approach based on $Z^2$-contrast can be misleading if for instance in certain less compact structures electron channeling effects are not correctly taken into account.

Over the last 3 years, we have established a global research collaboration anchored around electron microscopists at USC (Thomas Vogt, Douglas Blom) and other people such as Angus Kirkland (Oxford), Nigel Browning (UC Davis and LLNL) with mathematicians at USC’s Interdisciplinary Mathematics Institute (Peter Binev, Robert Sharpley), Ronald DeVore (Texas A&M) and Wolfgang Dahmen (RWTH Aachen). These collaborations are critical in exploring novel denoising,
nonlocal algorithms as well as new methods to exploit Compressed Sensing for nanoscale chemical imaging. This book is to be seen as a progress report on these efforts.

We thought it was helpful to have Professor Michael Dickson (Philosophy, University of South Carolina) address issues of realism and perception of nano-images and how we might think of them in a “Kantian” way.

Chapters 2 and 3 are from well-established practitioners in the field of scanning transmission electron microscopy, led by Professors Nigel Browning and Angus Kirkland from the University of California Davis and Oxford University, respectively. Both chapters exemplify what it means to “image at the edge” and push the method to its current limitations. Limitations that might be pushed back a bit further using different image analysis techniques.

Chapters 4 and 5 rely heavily on two facilities at USC: many experimental data were taken on a JEOL JEM-2100F (200 kV) microscope with field emission gun, spherical aberration corrector, STEM mode, High Angle Annular Dark Field detector (HAADF), EELS, EDX, and tomography mode. This instrument provides routinely sub-Angstrom image resolution and elemental resolution at the atomic level and is operated by Dr. Douglas Blom. Second, we have a state-of-the-art floating-point parallel computing cluster based on general purpose graphics processing units (GPGPUs) achieved through parallel architecture of the GPGPU, which is a mini-supercomputer packed in a graphics card used for floating point operations. Our major electron imaging simulation code is written in the CUDA programming language which uses a single-precision FFT routine in the CUFFT library. We have been able to simulate inorganic structures of unprecedented complexity using this hardware. These simulations were performed by Sonali Mitra a Ph.D. student working under the supervision of Drs. Vogt and Blom in the Department of Chemistry and Biochemistry at the University of South Carolina.

The work by Amit Singer and Yoel Shkolnisky (Chap. 6) is a tour-de-force in explaining the mathematical theory cryo-transmission electron microscopy is based on. What appears to many practitioners of electron microscopy as “black art” is deeply rooted in fundamental mathematics. This chapter illustrates the deep-rooted connections between imaging and applied mathematics, illustrating what Eugene Wigner coined in 1960 as the “unreasonable effectiveness of mathematics in the natural sciences” (Communications on Pure and Applied Mathematics 13 (1): 1–14).

We believe that the combination of state-of-the-art imaging using aberration-corrected electron microscopy with applied and computational mathematics will enable a “new age” of imaging in both the hard and soft sciences. This will leverage the huge infrastructure investments that have been made globally over the past 10 years in national laboratories, universities, and selected companies.

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