ELSEVIER

Ultramicroscopy 90 (2001) 1–6

ultramicroscopy

www.elsevier.com/locate/ultramic

Lensless imaging: a workshop on "new approaches to the phase problem for non-periodic objects"

John C.H. Spence[a,*], M. Howells[b], L.D. Marks[c], J. Miao[d]

[a] Department of Physics, Arizona State University, Tempe, AZ 85287, USA
[b] Lawrence Berkeley Laboratory, Berkeley, CA 94720, USA
[c] Materials Science, Northwestern University, Evanston IL 60208, USA
[d] Stanford Linear Accelerator Center, Stanford University, Palo Alto, CA, USA

Received 5 July 2001

Abstract

Over the past two decades, theoretical tools and algorithms have been developed which, under not very restrictive conditions, allow the reconstruction of images from diffraction patterns of non-periodic objects. These methods promise lensless imaging for any radiation, free of aberrations, with wavelength-limited resolution. Recent experimental successes prompted an interdisciplinary international workshop on this topic at the Lawrence Berkeley National Laboratory, Berkeley, CA, USA, on May 17–19 2001, supported by the DOE, LBL and the Advanced Light Source. Our aim was to review the field, and to stimulate communication between the Signal Recovery, Coherent Optics, X-ray, Electron Microscopy and Applied Mathematics communities. The results are summarized in this paper and on the web. A second workshop is planned for 2003. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Lensless imaging; Phase problem; Non-periodic objects

1. Introduction

It is a remarkable fact that, under not very restrictive conditions, the complex image of a finite object can be calculated from measurements of the scattered intensity in the far field (for a review of this field see Ref. [1]). In addition, non-interferometric methods now also exist which can reconstruct the same image from measurements of intensity across one or two planes in the near field. These reconstruction methods, developed over the last decade, offer imaging possibilities for new radiations for which no lenses exist, and in some cases promise wavelength-limited resolution without aberrations. The recent publication of experimental lensless image reconstructions using X-rays and neutrons has therefore excited considerable interest.

The theoretical basis and applications of these methods was the topic for a three-day interdisciplinary international workshop, held recently in Berkeley, CA, supported by the US Department of Energy, LBL and the Advanced Light Source, and organized by John Spence, Malcolm Howells, Laurie Marks and John Miao. The purpose of

*Corresponding author.
E-mail address: spence@asu.edu (J.C.H. Spence).

PII: S0304-3991(01)00128-0

the workshop, with about 70 participants, was to bring together researchers from the many fields who use these methods, with particular emphasis on new applications to X-ray, electron and neutron imaging. In particular, we felt that there was an opportunity for these areas to learn from the Signal Recovery, Coherent Optics, and Applied Mathematics communities, and that the connections between Holographic methods and iterative schemes, and between the Direct Methods of Crystallography (solvent flattening, density modification, for example) and the use of supports in iterative methods could be profitably developed. Recent applications of these methods have included the corrections of aberrations from Hubble Space Telescope images, lensless missile imaging, soft X-ray microscopy, medical imaging, synthetic aperture radar, electron microscopy and neutron imaging. Four related theoretical approaches lay behind most of the talks: (i) The Gerchberg–Saxton–Fienup algorithm; (We were delighted to have both Owen Saxton and Ralph Gerchberg present, both of whom spoke briefly of their current work.) (ii) The transport of intensity (ToI) methods developed by Nugent and others from Teague's early work. (iii) Approaches based on analytic continuation (developed by Fiddy and others), and (iv) The theory of Bregman projections onto convex sets, and extensions to the non-convex case. Altogether, we felt that a confluence of exciting new and old ideas were converging in the field of lensless imaging, and that recent experimental breakthroughs made this an appropriate time for an interdisciplinary conference.

2. The workshop

Overview talks on the first morning covered the main areas. J. Fienup reviewed applications over 25 years of his popular hybrid input–output (HiO) iterative algorithm to problems in astronomy, coherent and incoherent visible-light imaging, and defense imaging. The algorithm iterates between real and reciprocal space, applying known constraints in each domain, such as the known modulus of the transform of the wanted image, and includes a feedback feature based on control theory. The support of a function is defined as the region in which it is non-zero — the remarkable success of this robust algorithm depends on some knowledge of the support of the object, which may be estimated from the known autocorrelation function. The algorithm is fairly tolerant to noise, yet manages to find the thousands of unknown phases from a sampled diffraction pattern. This is usually achieved without stagnation, due to both the nature of the problem, and the algorithm's ability to climb out of local minima. P. Combettes then reviewed the problem from the point of view of non-convex set theory, based on his authoritative recent review article in Adv. Imag. Electr. Phys. (Images are represented by points in an n-dimensional Hilbert space, with one dimension for each pixel. Distances between points represent a goodness-of-fit or error metric, and projections are made between sets of images subject to different constraints, which define the boundaries of the set. Given that unique or equivalent solutions exist subject to two contraints, the length of projection vectors between the set boundaries diminish with every iteration, and converge to a solution only if the constraints are convex. Symmetry, sign and support are convex constraints; however, the known-modulus constraint is non-convex.) Combettes provided a general mathematical review, then proposed three interesting approaches to the "convexification" of the problem. (One of these — projecting onto sets of functions (images) whose Fourier magnitude is less than or equal to the known value — was tested numerically by Fienup during the workshop). The third speaker before coffee, K. Nugent, reviewed theory and applications of the TOI method, a powerful method for quantitative phasing of near-field images (without using interferometery) which, by redefining the concept of phase in terms of propagation, his group has extended to partially coherent conditions. Experimental results were presented for optical microscopy, coherent atom optics, X-ray imaging, and electron microscopy. The first differential interference contrast electron images and the first experimental example of a neutron phase-contrast image were shown. (Electron microscopists familiar with the projected-charge-density approximation will be familiar with a similar principle. Area detectors record defocussed images downstream of the object.) The method is capable of measuring phase values of any size, without unwrapping. Phase discontinuities (vorticies), which occur at intensity zeros were also considered, as in a later talk.

After coffee, Joachim Frank described his remarkable work on the determination of the three-dimensional structure of the *E-coli* ribosome (the macromolecule responsible for synthesizing proteins) by cryomicroscopy in TEM. This appears to be the most successful method for determining the three-dimensional structure of "hydrated" molecules which cannot be crystallized, an aim shared by many of the X-ray specialists at the conference. Many years of sustained effort have now yielded a resolution of better than 1 nm. This work was of great interest to X-ray users of the HiO algorithm, who are developing similar tomographic methods in attempts to reconstruct the three-dimensional charge density of a molecule from diffraction patterns of individual, randomly oriented molecules. The use of femtosecond pulsed beams is proposed, in order to reduce damage. (Such patterns may be available at future X-ray free-electron laser facilities.) A poster from Huldt et al. dealt with the related problem of aligning diffraction patterns rather than images from randomly oriented molecules.

Sessions on two and three-dimensional reconstruction using the HiO algorithm followed lunch. John Miao described the first experimental use of the HiO algorithm to soft X-ray data, in which images of lithographed symbols were reconstructed from the diffraction pattern intensities. Simulations were also demonstrated for the reconstruction of macromolecules in three-dimensions — it appears that the convergence of the HiO algorithm improves with dimension, a most important result. Here the iterations were performed using three-dimensional Fourier transforms. There was much discussion of the definition of "oversampling" in this connection. Bearing in mind that the autocorrelation of an object (whose transform we detect) is about twice as wide as the object itself, old hands from the signal recovery community felt that sampling the diffracted *intensity* distribution at its Nyquist density should not be called oversampling. Nevertheless, such sampling is at twice the Nyquist density of the diffracted field distribution, and has the effect of placing the object into a larger computational superlattice (thereby defining the support for an isolated object). This is an example of the point, first made by D. Sayre in 1952 (and reiterated in his talk) that Bragg sampling is a factor of two too low to represent the autocorrelation function of a molecule which fills a unit cell in a crystal. It is this use of sampling which is finer than the Bragg interval which enables the HiO and other modern iterative techniques to solve the phase problem. Miao demonstrated the performance of the HiO algorithm for various degrees of further oversampling, and demonstrated the effectiveness of using a sign constraint for the imaginary part of the refractive index. I. Robinson then described his group's experimental work on imaging the shapes of nanocrystals using coherent X-rays. The HiO algorithm is used to phase the continuous distribution of scattering around a Bragg peak from small crystals. Development is aimed at obtaining a three-dimensional image of strained crystals. C. Jacobsen then described his group's work on diffraction tomography of cells, using a zone plate to magnify an in-line hologram (out-of-focus image). The important point was made that since depth of field decreases as the square of lateral resolution, zone-plate images can only be regarded as projections if the object is sufficiently small. Three-dimensional reconstruction from such images will reach their limit for about 1 μm objects, for the highest resolution zone plates currently available. A poster from Shapiro et al. with this group described HiO reconstruction in combination with lower resolution zone-plate imaging to provide support information. The design of their cryogenic goniometer was outlined. D. Sayre then gave an historical perspective on crystallographic phase recovery, and outlined the theory of oversampling, in the above sense, for phase determination. The point was made in discussion that high rates of oversampling increases dose and hence damage (and demands on computing power).

J. Spence followed with examples from his group of the application of the HiO algorithm to experimental coherent high-energy electron diffraction data for image reconstruction (at about 2 nm resolution), and to visible light laser diffraction patterns. The use of the electron microscope probe as a support was discussed. Simulations for the application of the HiO algorithm to neutron scattering for phase contrast imaging were shown. The first day ended with a contribution from I. Vartaniants, in which the effects of partial spatial coherence on the experiments described above by Robinson were analyzed.

The second day of the conference was devoted to ToI methods and, later, to Theory. S. Wilkins began with an impressive survey of the experimental results his group has obtained in X-ray imaging by various means, including hard X-ray phase contrast imaging, use of microfocus X-ray sources to obtain a diverging and therefore magnifying beam for radiographic schemes. D. Paganin followed this with a description of the application of the non-interferometric ToI method to the Aharonov–Bohm phase, and to the Lorentz electron microscope imaging of superconducting vortices for the purpose of quantitative phase measurement. H. Faulkner followed with a talk on the phase vortices which occur in regions where intensity falls to zero, creating difficulties for the ToI method, which assumes a continuous phase. She described a method for dealing with these singularities by using a through-focus series (known as "phase diversity" in the signal recovery community). After lunch, the theory session commenced with a second talk on applications of the HiO algorithm by J. Fienup, replacing J. Borwein. R. Luke then analyzed in detail the relationship between the set theoretic and analytic approaches, with the aim of combining the best properties of both into a higher-order, more robust and efficient algorithm, with quadratic convergence. H. Bauschke then contributed a talk on alternating and cyclic projection methods for solving convex feasibility problems, including over-relaxed projections, with some discussion of the non-convex case and the problem of inconsistent constraints. Following the coffee break, R. Millane reviewed the phase problem for multidimensional and undersampled data, showing that while the problem is underdetermined in one dimension and well-determined in two, it is overdetermined in three. Millane then considered the crystallographic case, and ways in which additional non-crystallographic symmetries or diffuse scattering along certain directions (e.g from two-dimensional crystals or fibers) can be used to reduce undersampling. P. Rez followed with a matrix formulation of the Fienup HiO algorithm, comparing the number of unknowns and equations with the degree of oversampling.

M. Fiddy then provided an overview of the analytic approach, in which the diffraction pattern is treated as a function of a complex variable, and is completely determined by the location of its zeros, since bandlimited functions are analytic, and objects with compact support have analytic transforms. Since factorizability has proven impractical in the presence of noise, Fiddy's group have been exploring the approximation of an irreducible function by a factorizable one. Fiddy also pointed out that the set of all bandlimited functions having a given set of real zero crossings is convex. Algorithms and their applications, based on these ideas, were described. The day ended with a talk by S. Patch on phase unwrapping for MRI imaging, where an urgent need exists for more efficient methods.

The final day of the conference covered other approaches and links to the crystallographic phase problem. L. Marks started the day with a general review of the phase problem based on feasible sets, followed by more detailed treatment of some one-dimensional problems — the current through a Josephson junction, inversion of X-ray reflectivity data, and the use of the one-dimensional support together with crystallography constraints to phase diffraction patterns from surfaces. Marks also covered Fourier difference methods, non-convex sets of constraints which behave as though convex, listed some known convex and non-convex constraints, discussed use of direct methods, maximum entropy and atomicity as constraints, and the uniqueness of the difficult one-dimensional case. F. Chen then described his collaborative work on use of the G-S algorithm and maximum-entropy deconvolution to improve the resolution (to the sub-Angstrom level) of TEM atomic-structure images of SiC and $NiSi_2$/Si interfaces. After coffee, A. Szoke reviewed the principles of his group's "Eden" software, which makes extensive use of holographic principles, fragment completion, a Gaussian expansion, and atomicity constraints to solve the phase problem for crystals. A conjugate-gradient search is used to deal with the self-interference term in the holography equations, since the scattering from the reference structure is not dominant in general. The known fragment plays a similar role to the known (usually zero) density outside the support region in the HiO algorithm. Applications included Cu_2O, the ribosome at 0.5 nm resolution, and photoactive yellow protein, using oversampled data obtained from crystals containing two closely related molecules, one known. D. Saldin continued the theme of structure completion (in which a known fragment of a structure is used as a kind of holographic reference), using the examples of surface diffraction (where the bulk is known) and macromolecules (for which part is known). The maximum entropy method of Collins was also recast in the form of an HiO algorithm. K. Anduleit followed with a talk on the use of EDEN to solve for the electron density around Er dopants in Sc_2O_3 by X-ray diffuse scattering, treating the host crystal as a reference. The session closed with a talk by A. Rahmim, describing a collaboration in which striking images of anti-ferromagnetic and ferromagnetic domains in Co/Pt multilayers had been reconstructed from experimental resonant soft X-ray scattering (speckle) patterns. The magnetic X-ray scattering is obtained using circularly polarized X-rays, tuned to the Co L edge, taking differences between polarization directions. Reconstructions were obtained using HiO for both the reflection and transmission cases.

The final afternoon was devoted to the phase problem in crystallography and a late contribution from J. Rodenberg. T. Terwilliger described a likelihood approach to density modification in X-ray crystallography where the density at some points in the cell is known. Any prior knowledge of structure factors is combined with experimental data to form a combined likelihood function. It has become clear that the knowledge of object-plane values outside the support assumed in the non-periodic case is equivalent to the density modification techniques of crystallography, where the water-jacket (of known density) around a crystallized molecule plays the role of a support. John Rodenburg described how the phase problem is solved using Ptychography, in which a fine coherent probe is scanned over a periodic transmission sample in such a way that the diffraction orders overlap, and this solution was extended to non-periodic samples. Super-resolution schemes based on this principle have been demonstrated, which promise tomography with sub-Angstrom resolution. A. Urzhumtsev reviewed the use of minimized score functions in crystallography. A new ab initio phasing approach was described, and applications to the 50S ribosome and Lipoprotein were given. The last session of the conference commenced with a talk by Q. Shen on the reference-beam diffraction method for crystals, in which two Bragg-reflected beams are excited simultaneously in a geometry which allows many such three-beam interference profiles to be recorded on the same area detector. The interference amongst beams allows solution of the phase problem, with possible application to proteins. G. Xu then described a method of X-ray holography without a reference beam, a method of phase determination based on the asymmetry in Bragg rocking curves, and a study of this intensity close to the Bragg condition used to determine whether nanotubes are helically wound or are concentric cylinders. In the last talk, O. Terasaki described his collaborative work on mesoporous silicates, whose structures have been has solved by electron crystallography in three dimensions. The structures which form in the cages and intersticies of these crystals have also been solved. A combination of near-atomic-resolution imaging and diffraction are used to solve the phase problem.

Posters presented at the conference covered work by Huldt on alignment, averaging and reconstruction of single-particle diffraction patterns, two posters on internal source X-ray holography by Marchesini and co-workers, a poster by Shapiro and others on their three-dimensional X-ray diffraction microscope, one by Vincent on phase retrieval in TEM using Fresnel images, and one by Weierstall on image reconstruction using HiO applied to coherent visible-light diffracted intensities.

A second workshop on this topic is planned for summer 2003, to be organised by Prof. K. Nugent (Physics, Melbourne University, Victoria, Australia).

References

[1] H. Stark (Ed.), Image Recovery, Theory and Applications. Academic Press, New York, 1987. The abstracts and references to papers relevant to this conference can be found at http://www-esg.lbl.gov/esg/meetings/phasing/index.html.