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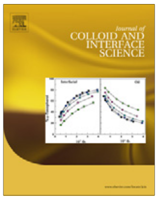

Feature Article

A new approach to the investigation of nanoparticles: Electron tomography with compressed sensing

John Meurig Thomas [a,*], Rowan Leary [a,*], Paul A. Midgley [a], Daniel J. Holland [b]

[a] Department of Materials Science and Metallurgy, University of Cambridge, Pembroke Street, Cambridge CB2 3QZ, UK
[b] Department of Chemical Engineering and Biotechnology, University of Cambridge, New Museums Site, Pembroke Street, Cambridge CB2 3RA, UK

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ABSTRACT

The principal purpose of this contribution is to illustrate the potential of compressed sensing electron tomography for the characterisation of nanoparticulate materials that are vulnerable to electron beam damage. Not only is there growing interest in nanoparticles of organic materials in medical and allied contexts, there is also the need to investigate nanoparticles and nanoclusters of metals supported on biological macromolecular entities in the context of drug delivery. A qualitative account of the principles of electron tomography is outlined with illustrations from the field of heterogeneous catalysis, where electron beam damage is less of an issue, and an appendix deals with more quantitative aspects of how compressed sensing promises to expand the range of samples that have hitherto been accessible to investigation.

1. Introduction

The technique of tomography is currently applied widely for the study of macro-objects in medicine and in engineering using X-rays or positrons as the probing radiation. In essence, tomography entails reconstructing the three-dimensional (3D) structure of an object from a series of two-dimensional (2D) projection images. Electron tomography (ET) is a relatively new tool for probing nanoparticulate and other nano-structured materials, but its use has grown rapidly in recent years, as may be gauged from Fig. 1.

Two of us (PAM and JMT) have hitherto exploited ET, which is capable of resolutions of *ca.* 10 Å, largely for the investigation of the morphologies, spatially-discriminating chemical compositions and defect properties of nanoclusters and nanoparticles of bimetallic heterogeneous catalysts [1–4]; but our group has also identified and demonstrated the power of the technique when allied to the so-called approach of compressed sensing (CS) – which we discuss below – for other kinds of investigation [5,6].

It is our conviction that ET allied to CS could contribute significantly to the now burgeoning field of nanoparticles in medicine and pharmacy, in which fine particles of entirely organic or biological materials – which are notoriously vulnerable to electron beam damage – are finding increasing use [7,8]. A very recent example entails the use of aggregates of poly(lactic-co-glycolic acid) nanoparticles to which are attached tissue plasminogen activator (*t*PA) for the treatment of atherosclerosis and the avoidance of blood clot formation during a stroke [8].

2. Methods

ET may be recorded either by the use of conventional transmission electron microscopy (TEM) under so-called bright-field (BF) illumination [9], or using high-angle annular dark-field scanning transmission electron microscopy (HAADF-STEM), the technique we favour. A diagrammatic summary is shown in Fig. 2. It has been shown elsewhere [10] that there are distinct advantages in using the HAADF mode in preference to the BF method. Moreover because the signal recorded under HAADF conditions directly reflects the atomic number (Z) contrast of the specimen, there are additional analytical advantages to be gained by utilising this mode. Indeed, Fig. 3 illustrates this point.

Qualitatively we may illustrate the essence of tomographic reconstruction with the diagrams shown in Fig. 2, where *inter alia*, the notion of back-projection is given, yielding a 3D reconstruction or 'tomogram.' Because of the practical limitations imposed by the relative disposition and size of the sample holder with respect to the pole-piece of the microscope, a so-called 'missing wedge' of

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* Corresponding authors. Fax: +44 (0)1223334567 (J.M. Thomas).
E-mail addresses: jmt2@cam.ac.uk (J.M. Thomas), rkl26@cam.ac.uk (R. Leary).

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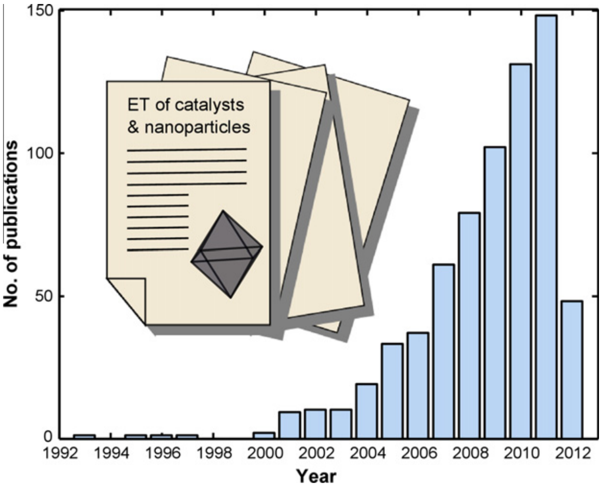

Fig. 1. The growing application of ET to the study of catalysts and nanoparticles, as tracked by the annual number of publications. *Source*: ISI Web of Knowledge, 02/08/12. Search term: "(electron tomography AND (catalyst* OR nanoparticle*))".

information is un-sampled by the tilt-series images and inevitably affects the reconstruction process. Elsewhere we have shown how quantitative ET may be carried out in the investigation of bimetallic nanocluster catalysts distributed over the inner surface of mesoporous silica [11]. A summary of the kind of information that may be retrieved is shown in Fig. 4.

We outline below (and explain in greater detail in the appendix) how, with CS, it is possible to retrieve valuable information pertaining to specimens that are vulnerable, to a greater or lesser extent, to electron beam damage, as well as specimens that, for other reasons, are not amenable to investigation by conventional ET. The actual examples of the use of CS-ET that we cite here are, in fact, ones that are relatively stable in the electron beam, but they serve as instructive proof-of-principle studies.

CS has arisen from information theorists and mathematicians concerned with signal retrieval. CS techniques are particularly useful in applications in which one cannot, for one reason or another, record a large number of measurements of the signal that is to be reconstructed. It has proven useful in magnetic resonance imaging (MRI) [12,13], for instance, and several accounts have been given detailing the essence of the 'compressive' measurement and recovery procedures [12,14–17].

The aim of CS is to recover a signal from fewer measurements than would normally be considered necessary, be it an angiogram in MRI, a spectrum in nuclear magnetic resonance, an image in astronomy, or a tomogram in ET. In order to reconstruct the signal from a small number of measurements, it is necessary to introduce some prior knowledge into the problem. In the case of CS, this prior knowledge is that the signal of interest is 'information limited' or 'sparse.' Here, 'information' refers to the number and location of non-zero elements in the signal. A signal is said to be 'sparse' if the number of non-zero elements is significantly less than the total number of elements comprising the signal. In the context of ET, these non-zero elements would most readily correspond to voxels (volume pixels) in the tomogram.

However, what makes CS so powerful is that it is not necessary for the signal itself to be sparse; instead the signal can be transformed into some other domain in which it is sparse. CS uses the idea that signals can be represented sparsely to recover images from incompletely sampled data by finding the sparsest solution that is consistent with the measured data.

In order to apply CS it is essential that the measurements are 'incoherent' with respect to the basis in which the signal is sparsely represented. This entails two aspects: (1) each data point measured must contain information about many of the elements that comprise the final signal, and (2) any artefacts arising from incomplete measurements should appear noise-like (i.e. not be sparse) in the domain in which the signal is represented sparsely. The first of these two points is readily addressed by ET data sets, as each measurement will comprise a projection through the sample and therefore contain information about every part of the sample through which the electron beam has passed. The second point is more difficult to conceptualise, but essentially means that artefacts that arise from incomplete sampling from any one part of a signal should be spread throughout as much of the remainder of the

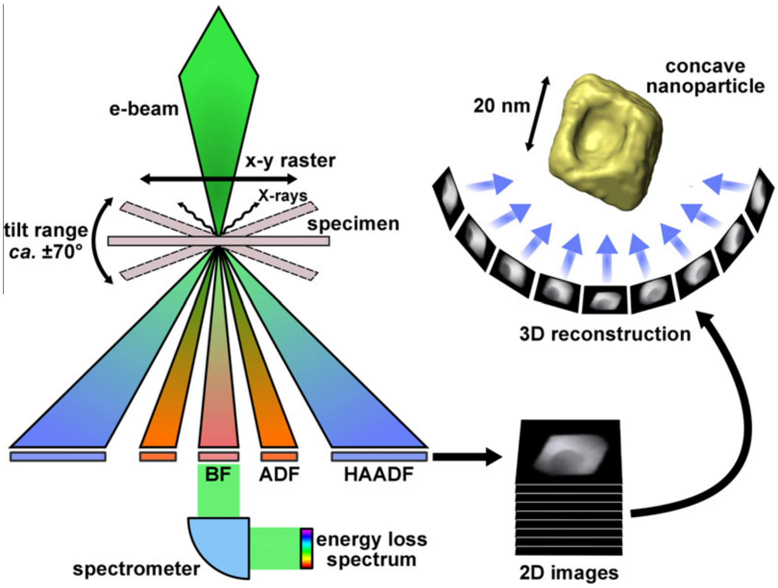

Fig. 2. The essence of ET: an angular series of 2D projection images is recorded by tilting the specimen in the (scanning) transmission electron microscope. The 'tilt-series' of images are then back-projected into space to obtain a 3D reconstruction. A variety of signals may be recorded, including bright-field (BF), annular dark-field (ADF) and high-angle annular dark-field (HAADF) signals. The BF detector can be removed to allow the transmitted electrons to pass through to a spectrometer and form an energy-loss spectrum.