LETTER

Reply to Wang and Yu: Both electron lambda tomography and interior tomography have their uses

Wang and Yu (1) suggest that interior tomography (IT) (2) could outperform electron lambda tomography (ELT) (3) for electron tomography (ET) data. We suggest that IT could be useful for in vitro specimens (isolated macromolecular complexes in water) whereas ELT has been shown to be useful for in situ specimens (macromolecular complexes in complex cellular environments, as in tissue). We suggest that the tests reported in ref. 1 are not necessarily relevant to ET, although ET reconstructions of Rullgård (4) and Öktem suggest that IT might perform well on in vitro data.

(*i*) The main issues in ET are shot noise and clutter. Data are very noisy and the signal often has low-contrast against the background. The examples shown by Wang and Yu demonstrate that IT is effective on problems in which the signal has high contrast and data are low-noise or noise-free. Therefore, they do not demonstrate that IT outperforms ELT for ET, even though they demonstrate excellent performance for low-noise, high-contrast data. The good performance of ELT in ET originates mainly from ELT overemphasizing visible singularities and thereby increasing the contrast in the reconstructed signal (5).

(*ii*) We suggest that not all of the assumptions of IT are valid for ET. IT uses compressive sensing, which is based on the principle that a signal that is sparse with respect to some frame/basis is exactly recoverable with overwhelming probability from limited noise-free data whenever the measurement matrix fulfills the restricted isometry property (RIP). In limited angle tomography, the RIP does not hold, so the aforementioned principle does not apply to ET. Similarly, the uniqueness results in ref. 2 do not seem to apply to the limited-angle setting in ET. Furthermore, in ref. 2, uniqueness is proved by means of analytic continuation, an ill-posed procedure. IT gives exact reconstruction, with exact data, under assumptions that do not necessarily hold for ET data.

(*iii*) Our experience with TV regularization applied to ET, i.e., with IT, is that it can perform well on in vitro specimens by suppressing the background clutter (4). However, for in situ specimens, our experience suggests that the advantage of using IT is negligible compared with standard methods. The reason IT does not seem to be better for in situ specimens is probably that such specimens do not necessarily have a sparse gradient.

IT may be superior to ELT for in vitro specimens, but it needs to be tested on real ET data rather than on low-noise computed tomography (CT) data. ELT performs the best for in situ specimens where our experience shows that IT reconstructions can be hampered by severe staircasing (Fig. 1*iii*). This problem might be overcome, but our experience suggests that would require modifying the TV function as in ref. 6. Most importantly, however, is that the signal-to-noise ratio is much smaller in ET data and that data, especially in situ ET data, are much more cluttered than the standard CT data on which IT is so effective.

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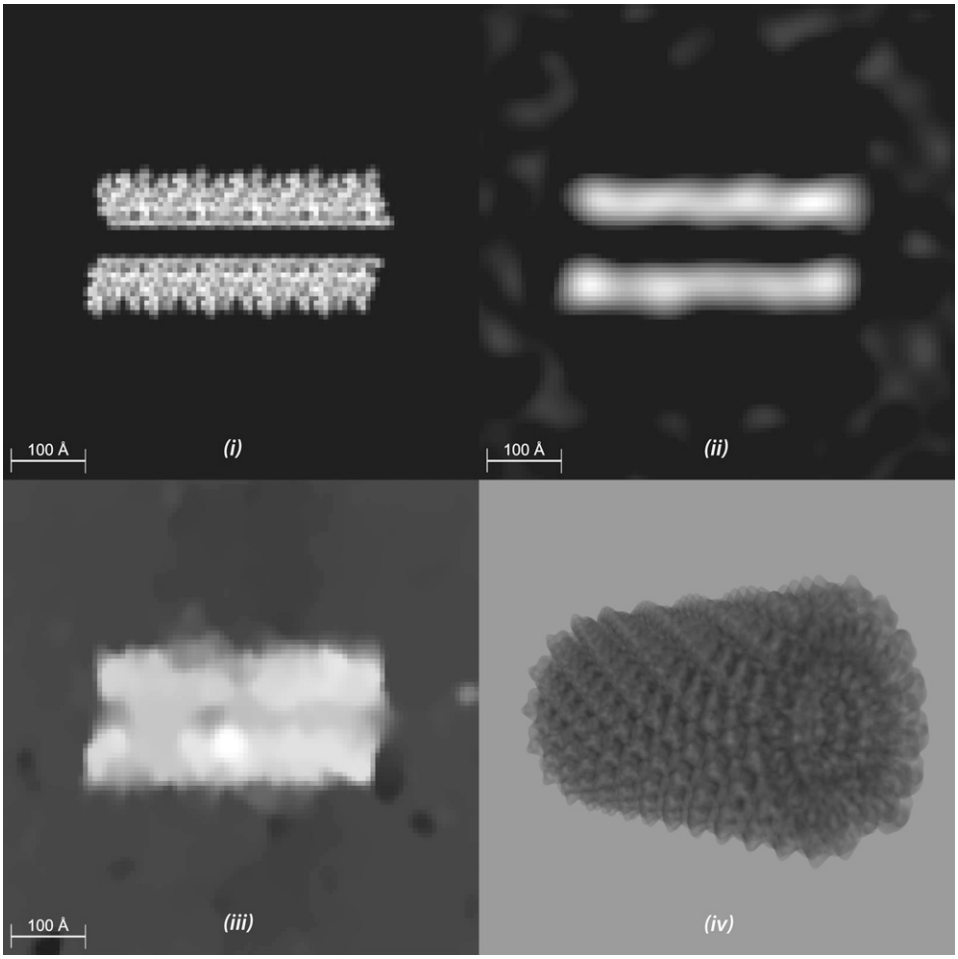

Fig. 1. Reconstructions from simulated data of an in vitro specimen containing tobacco mosaic virus (TMV). (*i*) A slice through the TMV phantom shown in *iv*. (*ii*) The best filtered backprojection reconstruction. (*iii*) The best IT reconstructions. It is clear that the central canal in the TMV is occluded in the IT reconstruction in *iii* due to staircasing. The simulated ET data are from H. Rullgård, Stockholm University.