Automated *de novo* Electron Density Map Tracing for the Structural Genomics Era

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Structural genomics initiatives around the world have gained momentum in recent years. An early step in such projects is the tracing of initial electron density maps, and this remains a challenging step requiring significant expertise. Map interpretation is especially demanding at lower resolutions, or when there are errors associated with the phase information. Two methods of tracing electron density maps have been implemented in the crystallographic modeling environment, QUANTA. The first method is optimal for high-resolution (≥ 2.0 Å) data sets, and involves simultaneous multiple-path analysis to identify the optimal path of the protein chain in skeletonized representations of electron density maps. In the second method, a secondary structure pattern analysis of skeletonized electron density maps is carried out, and then the secondary structure elements (alpha helices and beta strands) are converted to an all alpha-carbon representation, and extended to structural features such as turns and loops. The second method improves on the limitations of existing auto-tracing programs by extending the effective low-resolution limits from ~ 2.9 Å to ~ 4.0 Å.

Here we present results of the two tracing methods when applied to datasets with different resolution limits and figures of merit. The resultant alpha carbon traces, as well as all-atom models (built with QUANTA), are compared to the respective published structures. The two methods are extremely robust and fast (less than a second for the high-resolution tracing, and less than five minutes for the low-resolution tracing), and can trace the majority of alpha carbons in electron density maps with figures of merit as low as 0.5.

Keywords: de novo map tracing, x-ray crystallography software, automation in crystallography