INTRODUCTION

Current development of methods for solving macromolecular structures is largely focused on high-resolution data. However, many of the most challenging questions, which have to be addressed by modern structural biology, require an analysis of large macromolecular complexes, for which only in rare cases high-resolution data can be obtained.

The interpretation of very low-resolution data (>10 Å) usually starts with the segmentation of the map (e.g., Watershed algorithm), which does not always give satisfactory results. Overall, fitting of known structures currently requires a lot of human expert knowledge and interaction. Instead, an automated objective procedure is highly desirable.

METHOD

We use 3rd-order moment invariants to identify regions in density maps of macromolecular complexes that match known structures or their fragments. False positives are eliminated using difference distance matrices. As a result, the structures of the fragments are placed into the map.

Third-order moment invariants give a concise but comprehensive description of 3D objects, providing convenient means for fast searches through a large amount of 3D data.

RESULTS

The method has been tested on calculated density maps for large macromolecular complex of GroEL with high-resolution limit between 10 and 20 Å. The individual domains were placed in the low-resolution density maps with an average RMSD on Cα atoms of 2.2 Å at 10 Å resolution.

CONCLUSION

For the last decade there have been many attempts to develop reliable 3D map segmentation algorithms with varying success, in order to reduce the complexity of the challenging task of low-resolution density map interpretation. The method presented here does not require a map segmentation step and provides accurate results without human interaction in reasonable time, due to the use of sophisticated pattern recognition algorithms. Implementation of real-space refinement procedures is expected to improve the results even further.