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Three-dimensional electron microscopy and molecular modelling studies of a spiral-forming biocatalyst

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<p>Nitrilase and amidase enzymes catalyse the conversion of nitriles and amides to their corresponding acid and ammonia - chemistry which is useful in synthesis of drug compounds and fine chemicals. The conversion of cyanide, a nitrile, to ammonia and formic acid is useful in detoxification of contaminated wastewater. The cyanide dihydratase from Bacillus pumilus (CynDpum) catalyses this reaction and is thus a potentially useful biocatalyst. CynDpum and related nitrilase enzymes become activated by formation of spiral-shaped multimers. Evidence suggests that multimer formation regulates activity, by mechanisms which are still not clear. We have used a combination of transmission electron microscopy (EM) with 3-D image reconstruction, molecular modelling, and mutagenesis to investigate the mechanism of helix formation in CynDpum. We have implemented a new routine in the molecular dynamics package, NAMD, that allows helical symmetry to be used as a constraint, together with the EM volume. This method improves on asymmetrical modelling procedures and has aided in our atomic-level interpretation of low-resolution 3-D maps from negative-stain EM. This in turn has allowed us to make testable predictions about the importance of specific amino acids for the mechanical stability of the spirals. We show that salt bridges in one interface are not required for complex formation, but that mutations in this area can enhance the mechanical stability of the enzyme.

Level (Hons, MSc,
   PhD, other)?

Postdoc

Consider for a student
   award (Yes / No)?

No

Would you like to
 submit a short paper
 for the Conference
 Proceedings (Yes / No)?

No

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