



Research Highlights

Nature Chemistry

Published online: 26 June 2009 | doi:10.1038/nchem.299

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Enzymology: Directing diffusion

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Complementary computational and experimental studies support a funnel-like model with multiple pathways for oxygen diffusion into flavoenzyme active sites

Flavoenzymes take part in many cellular processes and have a central role in aerobic metabolism. As their name suggests they contain a flavin cofactor and its reaction with oxygen is a key step in many of these processes. Exactly how oxygen molecules arrive at the enzyme active site is currently under debate: is it simply passive diffusion or is it guided by the protein? If it is guided, then can the molecule take just one pathway or several?

Now Riccardo Baron from the University of California at San Diego and colleagues have studied¹ the diffusion pathways of oxygen in examples of two types of flavoenzymes: a monooxygenase and an oxidase. Using molecular dynamics they simulated 500 oxygen trajectories for each enzyme and found multiple pathways for both. In each enzyme the pathways led to the same defined active-site entry points, showing that oxygen diffusion is indeed guided by the protein using funnelling architectures.

The active-site entry points in each enzyme are made up of specific sets of residues that direct oxygen to the flavin cofactor. The importance of the environment local to the flavin was confirmed through understanding differences in reaction rates when key residues in each enzyme were replaced to create mutants.



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Reference

1. Baron, R. *et al.* Multiple pathways guide oxygen diffusion into flavoenzyme active sites. *Proc. Natl Acad. Sci. USA* doi:10.1073/pnas.0903809106 (2009) | [Article](#) |

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