

# Séminaire

**Conférencier interne**

Vendredi 17 Sept.2010

**A 11h - Salle des séminaires de l'IBS**

**Institut de Biologie Structurale J.P. Ebel**  
41, rue Jules Horowitz  
F-38027 GRENOBLE Cedex 1  
Tél. +33 (0)4 38 78 95 50 - Fax +33 (0)4 38 78 54 94  
[www.ibs.fr](http://www.ibs.fr)

**Par Colin Jackson**

**Institut de Biologie Structurale J.P.Ebel**  
Laboratoire d'Enzymologie Moléculaire (LEM)

## Following evolution at a molecular level

As formalized by Maynard-Smith, major evolutionary transitions of function and structure must occur gradually, and smoothly, through functional intermediates states. However, the nature of such transitions and intermediates remains largely unknown. To explore this process, we have used laboratory evolution to generate a complete trajectory: starting from a promiscuous aryl esterase activity ( $k_{cat}/K_M = 1.4 \times 10^2$ ),  $10^5$  fold less efficient than the native activity of a phosphotriesterase, incremental sequence changes gradually produced a smooth 'functional switch', involving a  $4 \times 10^8$ -fold reversal in the relative catalytic efficiencies, generating an efficient aryl esterase ( $k_{cat}/K_M = 5 \times 10^6$ ). Structural analysis has been used to investigate the structure-function relationship, revealing the 'smoothness' of the transition is based upon the ability of the protein to adopt a range of conformations with different catalytic properties. In this sense, evolution of new function can be viewed as a gradual shift in the conformational equilibrium of an enzyme, rather than a series of discrete changes.

Axe thématique :  
Nouvelles approches pour la biologie structurale intégrée