

Special UniCat Lecture

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Lecturer: **Dr. Florian Hollfelder**, Department of Biochemistry,
University of Cambridge, UK

Title: **Multiple Catalytic Promiscuity:
Towards Rules and Tools**

Abstract: 'Promiscuous' enzymes possess additional activities on top of their native ones. We demonstrate this principle with observations of strong promiscuous activities with rate accelerations between 10^9 and 10^{15} . Promiscuity of these enzymes is not limited to a single activity, but allows the same active site to catalyse up to six additional activities. Promiscuous activities could be remnants from the evolutionary ancestor that has been gene duplicated and adapted to fulfill a new function. Alternatively the observation of promiscuity could indicate that an enzyme is 'pregnant' with another activity, i.e. has the potential to be mutated or evolved into a new catalyst. We probe this thesis by defining functional relationships in enzyme superfamilies, backwards by analysis of their phylogeny and 'forward' by directed evolution. This analysis is underpinned by structural and kinetic data on members of this superfamily. Finally, a new technology in which picoliter water-in-oil emulsion droplets produced in microfluidic devices are used as high-throughput screening reactors to generate fitness landscapes of enzymes as they evolve.

- van Loo, B.; Jonas, S.; Babbie, A. C.; Benjdia, A.; Berteau, O.; Hyvönen, M.; Hollfelder, F., An efficient, multiply promiscuous hydrolase in the alkaline phosphatase superfamily. *Proc. Natl Acad. Sci USA* **2010**, *107* (7), 2740-5.
- Villiers, B. R.; Hollfelder, F., Narrowing the Size Selectivity of an A-domain by Directed Evolution. *Chemistry & Biology* **2011**, *18*(10):1290-9.
- Kintsjes, B.; Picoliter Cell Lysate Assays in Microfluidic Droplet Compartments for Directed Enzyme Evolution. *Chem. & Biol.* **2012**, *in the press*.
- Schaerli, Y.; Hollfelder, F., The potential of microfluidic water-in-oil droplets in experimental biology. *Mol Bio Sys* **2009**, *5* (12), 1392-404.
- Babbie, A. C.; Tokuriki, N.; Hollfelder, F., What makes an enzyme promiscuous? *Curr. Op. Chem. Biol* **2010**, *14* (2), 200-7.
- Kintsjes, B.; van Vliet, L.; Devenish, S.; Hollfelder, F., Microfluidic Droplets: New Integrated Workflows for Biological Experiments. *Curr. Op. Chem. Biol.* **2010**, *14* (5), 548-55.

Date: **Tuesday, July 24, 2012**

Time: **9:15 pm - around 10:15 am**

Location: **TU Berlin, Institute of Chemistry
Straße des 17. Juni 115, 10623 Berlin
Building C, Lecture Hall C 264**

Organizer: **Jennifer Jaitzig (TUB) and Lars Lauterbach (HUB)**

Coffee and tea will be served thirty minutes prior to the lecture start.
Guests are cordially invited to attend!

Prof. Dr. Matthias Driess, Chair of the Cluster of Excellence UniCat