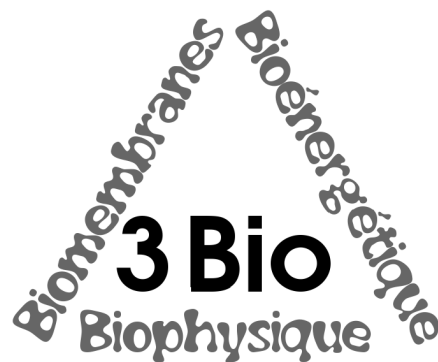


Séminaire du Service de Bioénergétique,  
Biologie Structurale et Mécanismes  
CEA/Saclay  
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**vendredi 30 septembre 2011 à 11h00, Bât. 532 P. 204**

## **Designing Functional Metalloproteins: Exploring the Roles of Non-covalent Interactions in Conferring and Fine-tuning Enzymatic Activities**

**Yi LU**

Department of Chemistry and Department of Biochemistry, University of Illinois, Urbana (USA)

Designing metalloproteins is an ultimate test of our knowledge about metalloproteins and can result in new biocatalysts for practical applications.<sup>1</sup> In this presentation, we provide three examples to demonstrate that, while reproducing the primary coordination sphere may be good enough to make structural models of metalloproteins, careful design of non-covalent secondary coordination sphere interactions is required to create functional metalloproteins. In the first example, we demonstrate fine-tuning of reduction potentials of azurin,<sup>2</sup> a member of cupredoxin family that are involved in long-range electron transfers in many important biological processes such as photosynthesis, to span ~1 V, through carefully design of hydrophobicity and hydrogen bonding networks around the primary coordination sphere, and the use of this powerful oxidant for asymmetric oxidation of organic substrates using water as the oxygen source. In the second example, we present evidence for the roles of two conserved glutamate residues in converting myoglobin into functional nitric oxide reductase, one through binding to the non-heme iron<sup>3</sup> and the other through hydrogen bonding interaction.<sup>4</sup> Finally, we show that the presence of tyrosine and associated hydrogen bonding network in a rationally designed heme-copper center of myoglobin is necessary to mimic heme-copper center in cytochrome c oxidase, resulting in a functional metalloenzyme that can catalyze the reduction of oxygen to water with over 1000 turnovers, and with minimal release of toxic reactive oxygen species such as superoxide and peroxide.

1. Yi Lu, Natasha Yeung, Nathan Sieracki and Nicholas M. Marshall, *Nature* 460, 855–862 (2009).

2. Nicholas M. Marshall, Dewain K. Garner, Tiffany D. Wilson, Yi-Gui Gao, Howard Robinson, Mark J. Nilges, and Yi Lu, *Nature* 462, 113–116 (2009).

3. Natasha Yeung, Ying-Wu Lin, Yi-Gui Gao, Xuan Zhao, Brandy S. Russell, Lanyu Lei, Kyle D. Miner, Howard Robinson, and Yi Lu, *Nature* 462, 1079–1082 (2009).

4. Ying-Wu Lin, Natasha Yeung, Yi-Gui Gao, Kyle D. Miner, Shiliang Tian, Howard Robinson, and Yi Lu, *Proc. Natl. Acad. Sci. USA* 107, 8581–8586 (2010).

**Invitation:** Anabella Ivancich

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