Unraveling the mechanism of multicopper oxidases : from ensemble to single molecule

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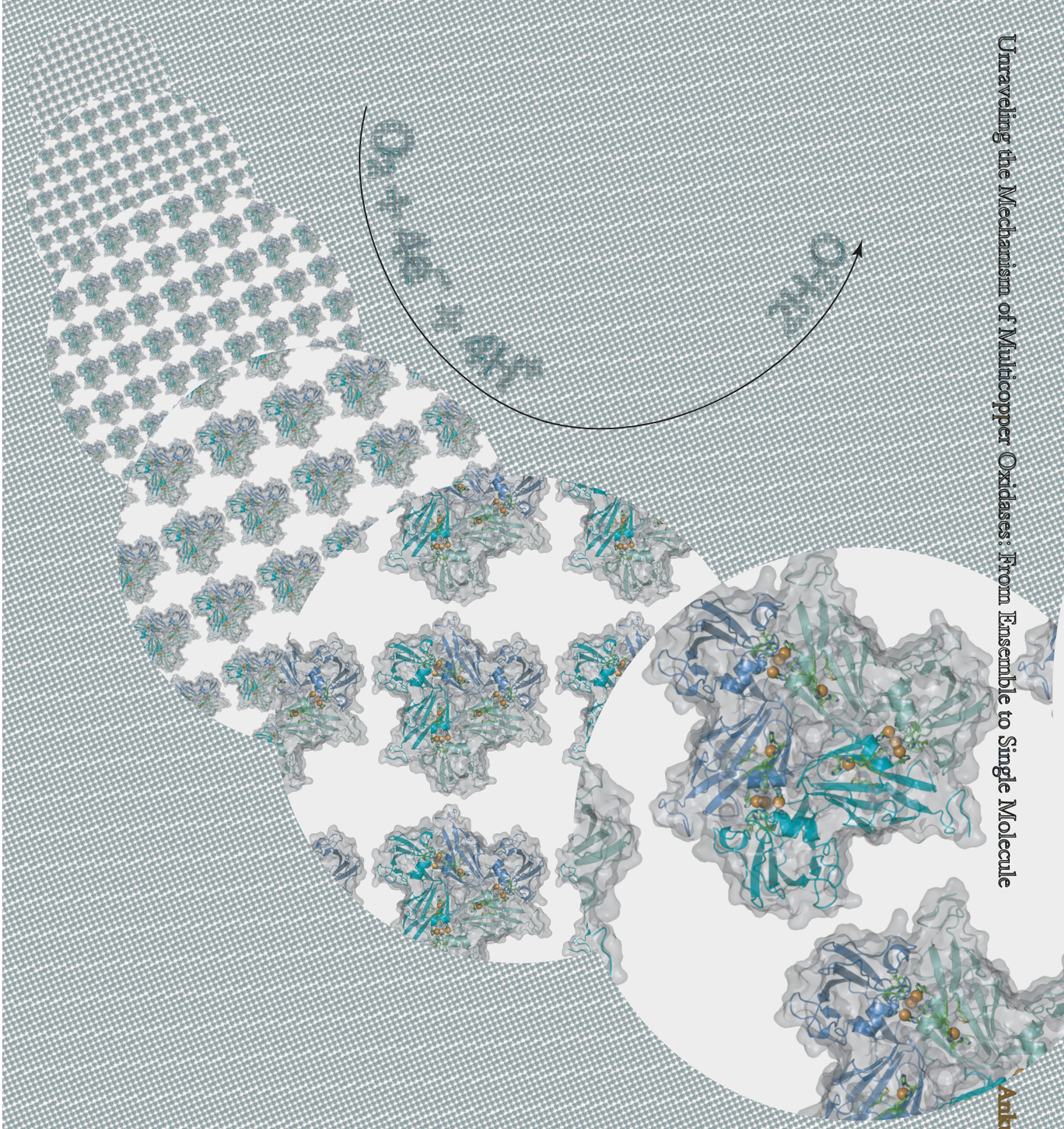

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Ankur Gupta

2014

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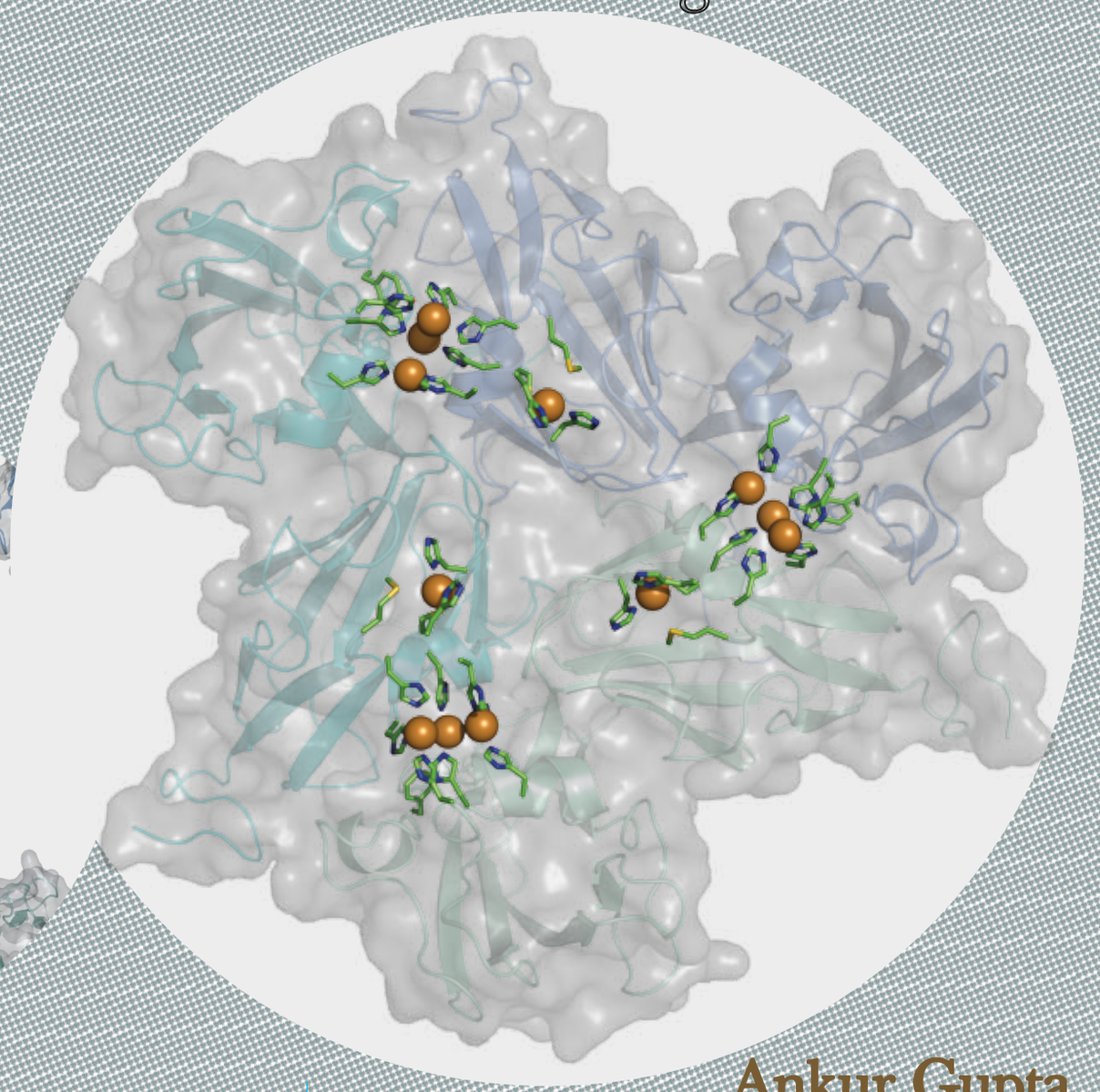

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Propositions

accompanying the thesis

"Unraveling the Mechanism of Multicopper Oxidases: From Ensemble to Single Molecule"

1. It is likely that the protein small laccase utilizes a redox-active tyrosine residue (Y108) to transiently provide one electron towards O_2 reduction at the trinuclear Cu cluster (TNC) when there is a shortage of the reducing equivalents in the milieu. (*This thesis, Chapter 2*)

2. The small laccase protein containing only three Cu ions per monomer can catalyze four-electron reduction of O_2 to H_2O. (*This thesis, Chapter 3*)

3. From a functional viewpoint, it is questionable that the type 2 Cu site evolved before the binuclear type 3 Cu site in multicopper proteins. (*Nakamura, K. et al. Cell. Mol. Life Sci. 2005, 62, 2050; This thesis, Chapter 3*)

4. A small spread in the activation energy among a population of molecules is sufficient to explain more than one order of magnitude spread in the associated electron transfer rate constants. (*This thesis, Chapter 4*)

5. Internal dynamics of enzymes are best studied under steady-state conditions. (*This thesis, Chapter 4*)

6. Solomon and coworkers, through mutagenesis and spectroscopic studies, have postulated that the asymmetry at the active site is responsible for the nature of O_2 binding; however, they don't clearly evaluate how their mutations disturb the active site. (*Augustine, A.J. et al. J. Am. Chem. Soc. 2010, 132, 6057*)

7. The rates of intramolecular electron transfer evaluated from single-molecule measurements of Cu-containing nitrite reductases are too low to be compatible with ensemble steady-state measurements. (*Kuznetsova S. et al. PNAS, 2008, 105, 3250; Goldsmith R.H. et al. PNAS, 2011, 108, 17269*)

8. The measurements of intermolecular electron transfer kinetics on the variants of putidaredoxin and cytochrome P450 reveal the role of polar residues in partner recognition. (*Hiruma, Y. et al. ChemBioChem, 2014, 15, 80*)

9. Binning of single–molecule time trajectories shall be avoided as much as possible. (*Watkins, L.P. et al. J. Phys. Chem. B, 2005, 109, 617*)

10. Despite the widespread use of aminosilanes for surface functionalization, there exists no standard to assess the surface wettability of a silanized surface.

11. Self–plagiarism is not plagiarism.

Ankur Gupta
Leiden, April 29, 2014