Hagen Hofmann et al., J Proteomics Bioinform 2017, 10:8(Suppl)
DOI: 10.4172/0974-276X-C1-0100



## Slow domain reconfiguration causes power law kinetics in a two-state enzyme

**Hagen Hofmann, Iris Grossman Haham, Gabriel Rosenblum** and **Trishool Namani**
Weizmann Institute of Science, Israel

Conformational transitions in proteins are typically captured well by rate equations that predict exponential kinetics for two-state reactions. Here, we describe a remarkable exception. The electron-transfer enzyme quiescin sulfhydryl oxidase (QSOX), a natural fusion of two functionally distinct domains, switches between open and closed domain arrangements with apparent power law kinetics. Using single-molecule Foerster resonance energy transfer (FRET) experiments on timescales from nanoseconds to milliseconds, we showed that the unusual open-close kinetics results from slow domain rearrangements in a heterogeneous ensemble of open conformers. While substrate accelerates the kinetics, thus suggesting a substrate-induced switch to an alternative free energy landscape of the enzyme, the power-law behavior is also preserved upon electron load. Our results show that conformational multiplicity with slow sampling dominates the motions of QSOX, thus providing an explanation for catalytic memory effects in other enzymes.

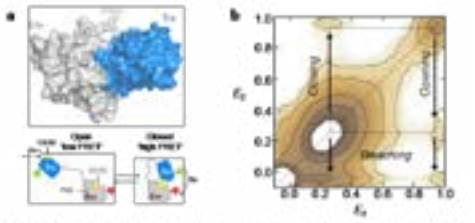

Figure 1: Structure of TbQSOX and domain motions measured with single-molecule FRET. (a) Structure of the enzyme TbQSOX in the closed conformation with Trx domain (blue) and Erv-domain (gray) docked to each other and schematic representation of the open and closed state that correspond to populations with low and high FRET, respectively. (b) Two-dimensional occurrence map for TbQSOX. Off-diagonal cross-peaks arise from opening/closing dynamics of the domains of the enzyme.

### Biography

Hagen Hofmann received his PhD from the Martin Luther University Halle-Wittenberg (Germany) in 2008. In the period 2008 - 2014, he was a Postdoctoral Fellow at the University of Zurich in the group of Benjamin Schuler and since 2014 he is heading the "Molecular Systems Biophysics" group at the Weizmann Institute of Science (Israel). He and his group use a broad set of single-molecule fluorescence tools to understand the dynamics of proteins and protein networks on timescales from nanoseconds to hours. In addition, live-cell imaging, *in vivo* single-molecule FRET, and single particle tracking is used to monitor proteins in live cells. His interest ranges from the physics of disordered proteins over coupled binding and folding reactions up to stochastic genetic circuits and regulatory protein networks.

hagen.hofmann@weizmann.ac.il

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