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PUBLISHING WITH THE PHYSICAL REVIEW AND PHYSICAL REVIEW LETTERS

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The American Physical Society (APS) is the publisher of the Physical Review and Physical Review Letters. The international scope of these publications increases annually, whereas the percentage of receipts from the U.S. has decreased to less than 1/3 of the total. In view of ever-increasing submissions from all over the world, it is of great importance to gather feedback from the international community regarding the journals and provide information about our publishing and peer review processes. In this presentation general information, submission statistics and publication statistics will be given. The dramatic growth of submissions, especially from Europe, over the past decade will be shown. The review process and the referee selection process will also be covered. Information about PROLA, which now includes all articles back to the beginnings of the Physical Review in 1893, and other APS online features for authors, referees and readers will also be included.
The aim of this presentation is to provide enough information to stimulate questions and discussion on a wide range of topics concerning publishing and peer review. Any feedback concerning the journals, the peer review process, or how the journals are perceived in the community is appreciated.

Keywords: PUBLISHING JOURNALS

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NOVEL PURIFICATION METHOD AND FIRST PRELIMINARY CRYSTALLISATION RESULTS OF ISOQUINOLINE-1-OXIDO-REDUCTASE (IOR) FROM P.DIMINUTA 7

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Isoquinoline-oxido-reductase (IOR) is a heterodimeric protein consisting of two subunits (80 kDa and 16 kDa). It is a member of the xanthine-oxidase (XO) family and contains a molybdopteridine in the active site and an iron-sulfur cluster inthe smaller subunit. IOR catalyses the first step of isoquinoline degradationthe oxidation of isoquinoline to 1-oxo-isoquinoline. The purification method established by M. Lehmann et. al. (1) involving heat-precipitation, a hydrophobic interaction column, cation-exchange with an S-sepharose column and gel filtration goes along with significant losses and shows poor reproducibility. For this reason it was necessary to find an alternative way of purification to obtain a pure IOR-sample suitable for crystallisation trials. This approach was largely hampered by IOR's instability at lower pHs and a complete loss of activity caused by anion-exchange chromatographic methods. The final purification method utilizes solely an S-sepharose column cation-exchange at pH 5.9 and gel filtration leading to highly pure IOR. Next to an increased yield a higher specific activity is observed. Clusters of needles were obtained in crystallisation trials. Currently the corresponding conditions are being optimised.
References
(1)Lehmann, M et. al. Purification and characterization of isoquinoline 1-oxidoreductase from Pseudomonas diminuta 7, a novel molybdenum-containing hydroxylase J.Biol. Chem 269 pp 11254-11260 (1994)

Keywords: **ISOQUINOLINE, MOLYBDENUM ENZYME, XANTHINE OXIDASE FAMILY**

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TIME RESOLVED X-RAY ABSORPTION SPECTROSCOPY STUDIES OF METALLOENZYMES REVEAL MECHANISTIC INFORMATION BEYOND KINETICS

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Metalloenzymes catalysis is usually mediated by distinct metal-substrate interactions, which provide the basis for their individual reaction mechanisms. However, elucidation of the intermediate structures and the electronic processes at the catalytic metal sites, which govern turnover, is often difficult to obtain. We have studied the metal site in a metalloenzyme by combining time resolved X-ray absorption spectroscopy, pre-steady state kinetic, and computational procedures. During turnover of the zinc metalloenzymes Thermoanaerobacter brockii alcohol dehydrogenase and matrix metalloproteinase, we detect a sequence of structural distortions in the coordination number of the catalytic zinc ion followed by concomitant changes in metal-ligand bond distances. This structural-dynamics correlates with the electronic perturbation of the metal site during turnover. The present results reveal new information about the reaction mechanism. Additionally, it provides novel means to study the role of metals in building up the catalytic power within the framework of the active site in metalloenzymes.

Keywords: **TIME RESOLVED, EXAFS, METALLOPROTEINS**

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CHANGES IN ACTIVE SITE GEOMETRY THROUGH NON ACTIVE SITE C95A MUTATION IN TETHERED HIV-1 PROTEASE HETERODIMER

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The emergence of drug-resistance through mutations in the HIV-1 protease enzyme is reducing the effectiveness of the designed inhibitors as drugs against AIDS. These mutations occur both within and away from the active site. To explore structural effects, we have mutated CYS95, which besides being a non active site residue is also highly conserved among various isolates of the virus. We report here X-ray structure of C95M/C1095A double mutant of tethered HIV-1 protease refined to 2.1 Å resolution (R-work = 19.5% and R-free = 26.1%). The unliganded structure shows closed flap conformations contradicting the belief that the flap is closed only in presence of an inhibitor. Comparison of the present structure with that of C95M single mutant reveals a shift of about 0.6 Å in the positions of the catalytic aspartates Asp25 and Asp1025 and the bound nucleophillic water. There is no repacking of residues around the site of mutation, leading to creation of an internal cavity and consequent destabilisation of the dimer. These changes in the active site geometry and stability are proposed to be the reason for the observed higher activity of this double mutant compared to the single mutant. We thus conclude that non active site mutations can exert influence by causing subtle changes in the active site geometry. This observation also provides a rationale for non active site drug resistance mutations.

Keywords: **HIV STRUCTURE MUTATION**