

# UniCat Colloquium

## PROF. STEVEN BOXER

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### *Vibrational Stark Spectroscopy Connects Electrostatics to Catalytic Rates at Enzyme Active Sites*

Electrostatic interactions impact every aspect of the structure and function of proteins, nucleic acids, and membranes. The transition states for many enzyme-catalyzed reactions involve a change in the distribution of charge relative to the starting material and/or products, and the selective stabilization of charge-separated transition states may be essential for catalysis.

The magnitudes of the electric fields in proteins and the variations in these fields at different sites are predicted to be enormous, but it is a challenge to obtain quantitative experimental information on these fields. We have developed vibrational Stark effect (VSE) spectroscopy to probe electrostatics and dynamics in organized systems, in particular in proteins where they can report on functionally important electric fields. The strategy involves deploying site-specific vibrational probes whose sensitivity to an electric field is measured in a calibrated external electric field by VSE spectroscopy. This gives the magnitude of the vibrational frequency shift associated with an electric field change in a protein, e.g. by making a mutation, changing pH, ligand binding, etc., projected along the bond axis, which is typically determined by x-ray crystallography. By measuring vibrational solvatochromism in conjunction with simulations, we obtain information on absolute fields and this can be applied to obtain information on functionally relevant electric fields at the active site of enzymes.

Using ketosteroid isomerase (KSI) as a model system, we correlate the field sensed at the bond involved in enzymatic catalysis with the rate of the reaction it catalyzes, including variations in this rate in a series of mutants. This provides the first direct connection between electric fields and function: for this system electrostatic interactions are a dominant contribution to catalytic proficiency. The concepts and methods described here can be extended to many other enzymes where data are already available, but a quantitative interpretation has been missing. This view of electric fields has been extended to provide a unifying description of non-covalent interactions, where now the vibrational Stark effect provides a physics-based method for measuring these fields.

**Wednesday, November 11, 2015 at 5:15 PM**

TU Berlin, Institute of Chemistry  
Straße des 17. Juni 115, 10623 Berlin

Building C, Lecture Hall **C 264**

**Prof. Hildebrandt (TUB)**

Organizer

Coffee and cake will be served 30 minutes before the lecture. Guests are cordially invited to attend!  
Prof. Dr. Matthias Driess - Chair of the Cluster of Excellence UniCat - [www.unicat.tu-berlin.de](http://www.unicat.tu-berlin.de)

