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## Novel IR spectroscopies to study biological membranes and membrane proteins

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## Abstract

Membrane proteins are the target of more than 50% of all drugs and are encoded by about 30% of the human genome. Electrophysiological techniques, like patch-clamp, unravelled many functional aspects of membrane proteins but suffer from structural sensitivity. We have developed Surface Enhanced Infrared Difference Absorption Spectroscopy (SEIDAS) to probe potential-induced structural changes of a protein on the level of a monolayer (see Ref. 1 for a recent review). A novel concept is introduced to incorporate membrane proteins into solid supported lipid bilayers in an orientated manner via the affinity of the His-tag to the Ni-NTA terminated gold surface. General applicability of the methodological approach is shown by tethering photosystem II to the gold surface. In conjunction with hydrogenase, the basis is set towards a biomimetic system for H<sub>2</sub>-production. FTIR difference spectra of a monolayer of sensory rhodopsin II were recorded under voltage-clamp conditions. This approach opens an avenue towards mechanistic studies of voltage-gated ion channels with unprecedented structural and temporal sensitivity. Finally, scanning near-field IR micrososcopy will be introduced and applied to study the structure of biomembranes<sup>2</sup>.

Vibrational spectroscopic studies on the novel light-gated channelrhodopsin-2 (ChR2) will be presented. ChR2 represents a versatile tool in the new field of optogenetics where physiological reactions are controlled by light. We have followed the structural changes of ChR2 by static and time-resolved FT-IR spectroscopy and identified internal proton transfer reactions involving aspartate and glutamate residues<sup>3</sup>. As the resolved protonation changes transiently alter the electrostatics and H-bonding networks within the protein, we infer that they represent the missing mechanistic link between retinal photo-isomerization and channel gating.

References:

1. Ataka, K., Stripp, S., and Heberle, J., Biochim. Biophys. Acta 1828, 2283 (2013)

2. Amenabar, I., Poly, S., Nuansing, W., Hubrich, E.H., Govyadinov, A., Huth, F., Krutokhvostov, R., Zhang, L., Knez, M., Heberle, J., Bittner, A., Hillenbrand, R., Nature Commun. **4**, 2890 (2013)

3. Lórenz-Fonfría, V.A., Resler, T., Krause, N., Nack, M., Gossing, M., Fischer von Mollard, G., Bamann, C., Bamberg, E., Schlesinger, R., and Heberle, J., Proc. Natl. Acad. Sci USA **110**, E1273-E1281 (2013)