

Highly sensitive coherent anti-stokes raman scattering imaging of protein crystals

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Serial crystallography at last generation X-ray synchrotron sources and free electron lasers enabled data collection with micrometer and even sub-micrometer size crystals which have resulted in amazing progress in structural biology.[1, 2] However, imaging of small crystals which although is highly demanded remains a challenge, especially in case of membrane protein crystals.

We describe here a new approach, based on polarized coherent anti-Stokes Raman scattering (P-CARS) imaging of *in meso* grown MP (and also water soluble protein) crystals. CARS microscopy provides an advanced nondestructive and label-free technique with high sensitivity and high lateral spatial resolution capable of selective chemical imaging of major types of macromolecules: proteins, lipids, nucleic acids, etc. Like spontaneous Raman, CARS probes vibrational modes in molecules and does not require exogenous dyes or markers, which is advantageous in imaging small molecules for which labeling may strongly affect their properties.

It is shown, that CARS, especially P-CARS, can be generally applied for fast, high resolution, high contrast and very informative imaging of protein crystals.

- [1] Cornelius Gati et al. (2014) Serial crystallography on *in vivo* grown microcrystals using synchrotron radiation. Vol 1, Part 2.
- [2] Haitao Zhang, et al. Structure of the Angiotensin Receptor Revealed by Serial Femtosecond Crystallography. (2015) Vol 161, Issue 4, Pages 833–844.