VU **University Amsterdam**

August 20, 2012

The Department of Physics and Astronomy at VU University / LaserLaB Amsterdam has an open **Ph.D. position** for the project **'Shedding light on the optogenetics toolbox'**, funded by the Netherlands Organization for Scientific Research (NWO) through the Council for Chemical Sciences (CW). The project will be carried out in the context of a VICI grant to Dr. John Kennis and involves time-resolved 2-dimensional infrared and stimulated Raman spectroscopy on optogenetic photosensory proteins.

We are looking for a candidate with a M.Sc. degree or equivalent in Physics, Physical Chemistry or Biophysics. Experience with advanced time-resolved optical spectroscopy is required.

We offer a 4-year position that is to result in a Ph.D. degree at the VU University. Salary and benefits are offered according to standard Dutch guidelines. The gross salary ranges from Eur 2042 per month in the first year and climbs to Eur 2612 in the fourth year, with vacation benefits of 8% of the annual salary. VU University furthermore offers a 13th month of salary.

All spectroscopic equipment to carry out the research is available at LaserLaB Amsterdam including four amplified Ti:sapphire laser systems complete with all necessary wavelength-conversion and detection equipment. This includes two newly installed pairs of synchronized amplified Ti:sapphire laser systems with optical excitation/infrared detection, as well as a stimulated Raman setup equipped with a tunable narrowband Raman pump source.

For further information please contact Dr. John Kennis, associate professor of Biophysics (j.t.m.kennis@vu.nl, +31 (0)20 5987212, www.nat.vu.nl/~john),

Project description:
In the past two decades, genetically encoded fluorescent proteins such as GFP have revolutionized the life sciences by enabling observation of cellular processes through fluorescence microscopy. Generalizing the concept of genetically encoded probes, a newly emerging field called 'optogenetics' is utilizing genetically encoded photoreceptor proteins to directly *control* cellular processes and organism behavior with light. The optogenetics toolbox includes LOV, BLUF and phytochrome

photoreceptors artificially fused to effector domains with desired function. In their native form, these photoreceptors occur fused or otherwise functionally connected with a wide variety of effector domains. This suggests that their photoswitching functionality proceeds through a specific set of interactions, a 'universal molecular language', which offers opportunities to engineer desired functionality in a rational way. This notion defines the scientific question to be addressed here: what is the molecular basis of the light-activated function of optogenetic switches? To predict if and how a photoreceptor protein will interact with the output domain of choice, one has to resolve structural changes from the moment of photoactivation on the picosecond-nanosecond timescale until their effector activation on the millisecond timescale. Until now, it has been very difficult to answer these questions, due to a lack of experimental methods with the appropriate timescales and specificity. Two novel structural-spectroscopic techniques, which are still in their infancy, Transient Stimulated Raman Spectroscopy and 2-Dimensional IR spectroscopy hold the promise to provide both structural and temporal resolution to unravel photo-initiated protein conformational changes. I propose to further develop these methods and apply them to unravel how optogenetic switches work. The proposed experiments will provide unique dynamic-structural insights in photoreceptor activation. In close conjunction with my collaborators that are pioneering the optogenetics field, judicious choices will be made in the rational design and improvement of novel optogenetic tools.