

Project Outline for PhD President's Research Scholarship in Bioimaging

Title: **Label-free multiphoton microscopy of intracellular lipids using Coherent Antistokes Raman Scattering (CARS)**

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Keywords: optical microscopy, bioimaging, lipids

Subject area: biophotonics

Brief Description:

The current first world “obesity epidemic” is a result of a reduction in physical activity and increase in calorie consumption as changes in modern lifestyle take place. Lipid storage mechanisms, which have evolved to allow animals to survive periods of nutrient deprivation, contribute to obesity resulting in clinical problems such as type 2 diabetes and atherosclerosis. The bulk of the excess energy derived from diet is stored as triacylglycerol, which can be efficiently packaged within mammalian cells as a cytosolic lipid droplet. However, still little is known about what controls the formation, trafficking and breakdown of lipid droplets in living cells.

Optical microscopy is still the only practical means of obtaining high spatial and temporal resolution within living cells and tissues. Coherent Antistokes Raman Scattering microscopy has recently emerged as a new multiphoton (ie nonlinear) microscopy technique which overcomes the need of fluorescent labelling and yet retains biomolecular specificity. CARS also features intrinsic spatial resolution in three dimensions (optical sectioning). This technique has proven to be very successful in imaging unstained lipid membranes and lipid vesicles via the Raman scattering of light with the stretching vibration of the dense carbon-hydrogen bonds in the aliphatic chain in lipids.

In collaboration with the School of Physics, we have built a CARS microscope that incorporates two-photon fluorescence and second harmonic generation for comparative/complementary studies. This project will develop correlative CARS/fluorescence microscopy to visualise unstained lipid droplets with CARS and associated protein components with two-photon fluorescence, in order to determine the dynamics of lipid droplet formation and development in living cells.

The project is suitable to graduates in either Physics or Biology and offers a unique cross-disciplinary training opportunity at the physics-life sciences interface. The student will be trained by Dr. Borri and Prof. Langbein who are internationally recognised for their innovative work in the development of CARS microscopy and have a strong track record in effectively supervising PhD students and by Dr. Watson who has several years of experience in immunofluorescence and live cell-imaging techniques.

References

Lars Kuerschner, Christine Moessinger, Christoph Thiele “Imaging of lipid biosynthesis: How a neutral lipid enters lipid droplets” *Traffic* **9**, 338-352 (2008).

Michiel Müller and Andreas Zumbusch, “Coherent anti-Stokes Raman Scattering Microscopy” *ChemPhysChem* **8**, 2156-2170 (2007).

Israel Rocha-Mendoza, Wolfgang Langbein, Peter Watson and Paola Borri “Differential Coherent antistokes Raman scattering Microscopy using linearly-chirped ultrafast laser pulses” *Optics Letters* **34**, 2258 (2009).

Funding notes:

The studentship is **fully-funded**, ie includes the payment of tuition fees at the Home/EU rate and a tax free maintenance stipend. Non-EU applicants are welcomed but successful applicants would have to self-fund the difference between the Home/EU and International Fee.

To fill an application form and for further information see:

<http://www.cardiff.ac.uk/presidents/bioimaging/index.html>

