# Molecular characterisation, modelling and prediction of organelle membrane dynamics in health and disease

**Supervisory team:**
**Main supervisor:** Prof Michael Schrader (University of Exeter)
**Second supervisor:** Prof Jeremy M. Henley (University of Bristol)
Dr Peter Petrov (University of Exeter), Dr David Richards (University of Exeter), Prof Peter Winlove (University of Exeter)

**Collaborators:** Prof Peter Ashwin (University of Exeter)

**Host institution:** University of Exeter (Streatham/St Luke's)

**Project description:**

Research on organelle membrane dynamics represents an exciting new field in modern cell biology and biomedical sciences because of its close relation to organelle functionality and its impact on developmental and physiological processes. Peroxisomes represent ideal model organelles as they have only one limiting membrane, can be easily labelled and are biochemically accessible. Vital, protective roles of peroxisomes in lipid metabolism, signalling, the combat of oxidative stress and ageing have emerged recently (Islinger & Schrader 2011, Curr Biol. 21:R800; Schrader et al. 2015, J Inherit Metab Dis 38:681).

Our work has revealed that peroxisomes are extremely dynamic and can be formed from pre-existing organelles by membrane growth and division, a model which is now generally accepted (Schrader et al. 2012, BBA 1822:1343). This requires remodelling of the peroxisomal membrane, the formation of tubular membrane extensions which subsequently constrict and divide into several new peroxisomes. Defects in membrane dynamics and multiplication of peroxisomes have been linked to novel disorders involving neurodegeneration, loss of sight and deafness (Delmaghani et al. 2015, Cell 163:894; Passmore 2020, BBA 1867:118709).

Recently, it was discovered that peroxisome interaction with other organelles, which depends on peroxisome number and membrane protrusion, is crucial for cholesterol distribution, lipid transfer and synthesis (Costello 2017, JCB 216:331; Schrader 2020, J Inherit Metab Dis 43:71). Overall, this highlights the importance of peroxisome dynamics for cell viability and human health. Despite their importance for cell physiology and homeostasis, the membrane dynamics of peroxisomes are not well understood and a biophysical model requires development.

This multi-disciplinary project combines cutting-edge biological, biophysical and modelling approaches to understand the mechanisms, principles and functions of organelle membrane dynamics in health and disease. This work will help to predict alterations in membrane dynamics and to propose treatments for patients with defects in organelle dynamics and related dysfunctions.