Membrane transport proteins as antimalarial drug targets

Membrane transport proteins – integral membrane proteins that mediate the passage of solutes across biological membranes – play a central role in cell ion homeostasis and signalling, nutrient uptake and the excretion of metabolic byproducts, as well as in the phenomenon of drug resistance. The human malaria parasite, Plasmodium falciparum, encodes over a hundred such proteins. High-throughput phenotypic screens of large chemical libraries for the ability to inhibit the in vitro growth of asexual intraerythrocytic malaria parasites have identified substantial numbers of potential antimalarial agents. Using a range of physiological assays developed to characterise malaria parasite membrane transport mechanisms we have investigated the mechanism of action of a range of chemically diverse antimalarial compounds identified in the high-throughput phenotypic screens. A significant number of these compounds have been found to disrupt membrane transport in the parasite, resulting in significant physiological and biochemical perturbations. The results are consistent with the view that membrane transport proteins offer particular opportunities as antimalarial drug targets. Two particular examples – PfATP4, a cation P-type ATPase implicated in parasite Na+ regulation, and PfFNT, a member of the formate-nitrite transporter family implicated in the efflux from the parasite of lactic acid – will be discussed.

Modelling the evolution of microbiomes

There has been a great deal of empirical work on the dynamics of microbiomes sampled from different compartments within hosts, between hosts, and between species. Formal theoretical work is now starting to emerge as well. In this talk, I will describe our computational framework for modelling the evolution of microbiomes. Our models take account of the acquisition of microbes from parents and/or the environment. We also model the constitution of the environmental microbial pool from which hosts can acquire their microbes [1]. We show how patterns of diversity change depending on the nature of microbial acquisition, and in the presence of selection acting on both hosts and microbes. If time permits, I will also discuss our most recent research on the short-term dynamics of microbes.