4D Microscopy of red blood cell membrane biophysics during Plasmodium falciparum invasion

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The symptoms of malaria are manifested during asexual blood stage of *Plasmodium* parasites, at the time of rapid multiplication of the parasite. This time window is a common target for the development of antimalarial therapies and potential vaccines. Difficulties in the development of efficient anti-malaria vaccines lie, in part, due to a fundamental lack of insight into the molecular processes and biophysical mechanisms which govern host-pathogen interactions at this stage. To this end, the distribution of important associated molecules during invasion of the red blood cell, has been studied by various microscopy techniques at fixed points in time [1, 2, 3]. The biophysical mechanisms for invasion have also been suggested through combined experimentation and modelling[4]. However, these studies lack the necessary temporal resolution to fully understand the molecular and biophysical basis for invasion in real time.

An important part of the invasion process is the formation of the parasitophorous vacuole membrane (PVM) at the point of entry to the host red blood cell. This membrane provides a physical barrier and an exchange surface between the parasite and the host cell. The formation of the PVM and subsequent remodelling of the host membrane during invasion are incredibly dynamic events and are very challenging to study in real time[5].

Presented in this study is a high-speed functional imaging method using resonant scanning confocal and lattice light sheet microscopy to determine the lipid order within parasite associated membranes during invasion. Using the ratiometric fluorescent dye Di-4-ANEPPS we show, for the first time, temporal changes in the physical properties of various membrane structures formed by the invading parasite. The combined spatial and temporal resolution of the imaging techniques used offers unprecedented insights into the dynamic processes of *Plasmodium* invasion of red blood cells.

References

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