Biomechanics and Biochemistry of Erythrocytes infected by Malaria Parasites

Collaborating researchers: Monica Diez, Sarah Eu, Zhangli Peng, and Ming Dao (Department of Material Science & Engineering, MIT)
Bridget Wall and Jacquin Niles (Department of Biological Engineering, MIT)
Yongkeun Park (KAIST, Korea)

LBRC researchers: Poorya Hosseini, Yongwoon Choi, Peter So and Zahid Yaqoob

Biomedical Background

During the intraerythrocytic development, the malaria parasite causes structural, biochemical, and mechanical changes to host red blood cells (RBCs). Major structural changes include the formation of parasitophorous vacuoles that surround the growing parasite in their host RBCs, loss of cell volume, and the appearance of small, nanoscale protrusions or “knobs,” on the membrane surface (1). From the biochemical standpoint, a considerable amount of hemoglobin (Hb) is digested by parasites during intraerythrocytic development and converted into insoluble polymerized forms of heme, known as hemozoin (2,3).

Two major mechanical modifications are loss of RBC deformability (4–6) and increased cytoadherence of the invaded RBC membrane to vascular endothelium and other RBCs (7). These changes lead to sequestration of RBCs in microvasculature in the later stages of parasite development, which is linked to vital organ dysfunction in severe malaria. In the earlier stage, where some loss of deformability occurs, Pf-RBCs continue to circulate in the bloodstream. Membrane dynamics of RBCs can be influenced by human disease states. These changes could provide insights into possible mechanistic pathways in the pathogenesis of malaria, because the parasite alters biophysical properties of RBCs during its intraerythrocyte stage that lasts up to 48 h.

Biophotonic Contributions

As noted above, parasitization by malaria-inducing Plasmodium falciparum leads to structural, biochemical, and mechanical modifications to the host red blood cells (RBCs). To study these modifications, one could investigate two intrinsic indicators: the refractive index and membrane fluctuations in parasite-invaded human RBCs. In previous research, we reported that there is experimental connections between these intrinsic indicators and pathological states (8). By employing two noninvasive optical techniques, tomographic phase microscopy and diffraction phase microscopy, we could extract three-dimensional maps of refractive index (Fig. 1) and nanoscale cell membrane fluctuations in isolated RBCs (Fig. 2), respectively. Our systematic experiments covered all intraerythrocytic stages of parasite development under physiological and febrile temperatures. These findings offer potential, and sufficiently general, avenues for identifying, through cell membrane dynamics, pathological states that cause or accompany human diseases. We are now exploring the effect of various transgenic parasites on the cell mechanics and biochemistry through developing new optical imaging techniques.
Three-dimensional refractive index maps of Pf-RBCs reveal the structural modifications and the hemoglobin concentration of cytoplasm. (A) Healthy RBC. (B) Ring stage. (C) Trophozoite stage. (D) Schizont stage.

Membrane fluctuations of Pf-RBCs of various stages at different temperatures.
Background Publications


Representative Collaborative Publications


Synergistic Funding

NIBIB, 9P41-EB015871-26A1
National Science Foundation Grant, DBI-0754339
Singapore-MIT Alliance for Research and Technology Center
Cambridge Foundation Fellowship
Samsung Scholarship
Whitaker Health Science Fellowship
Hamamatsu Photonics (Japan)