Ultrafast imaging unravels impact of hemoglobinopathy on dynamic shape recovery of malaria-infected erythrocytes

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Malaria still kills more than a half million people a year. Among various parasite strains, P.-falciparum is known to be the most lethal one. During their erythrocytic cycle (0 – 48 h post invation), parasites metabolize Hb, synthesize protein "knobs", and infected cells adhere onto the surface of blood vessel. It is well established that the genetic mutation of hemoglobin, known for example by sickle cell anemia (HbS), rescues patients from severe malaria, but the exact mechanism is still elusive.

My laboratory has been collaborating with parasitology group (led by Michael Lanzer) and theoretical physics (led by Ulrich Schwarz) to tackle this problem. Recently, we demonstrated that the modulation of knob size and density significantly affect the membrane-cytoskeleton coupling and effective membrane tension by the combination of the analysis of shape fluctuation and computer simulations [1]. With aid of single-cell chemical imaging of sub-cellular compartments, these findings could be attributed to the delayed proteolytic digestion of mutated hemoglobin, resulting in the differential knob expression and impaired remodeling of cytoskeletons [2].

In the poster, I will present our recent advances where we combine the self-built ultrafast imaging platform and simulated the splenic clearance in vitro, which is the place where infected erythrocytes were cleared in vivo. The imaging at a frame rate of 20 μs/frame (50 kHz) enables us to capture dynamic morphological phenotypes of infected human erythrocytes, which can be recapitulated by the SDPD simulations.

[1] B. Fröhlich, J. Jäger, C. Lansche, C. P. Sanchez, M. Cyrklaff, B. Buchholz, S. T. Soubeiga, J. Simpore, H. Ito, U. S. Schwarz, M. Lanzer, M. Tanaka, *Communications Biology* **2019**, 2, 311.

[2] B. Fröhlich, Y. Yang, J. Thoma, J. Czajor, C. Lansche, C. Sanchez, M. Lanzer, P. Cloetens, M. Tanaka, *Analytical Chemistry* **2020**, 92, 5765.