Cytoadhesion in malaria

Sebastian Sohn[1], Thorsten Auth[1], Bruce Caswell[2], George E. Karniadakis[2], Gerhard Gompper[1], Dmitry A. Fedosov[1]

[1]*Institute of Complex Systems and Institute for Advanced Simulation, Forschungszentrum Jülich, 52425, Jülich, Germany*

[2]*Division of Applied Mathematics, Brown University, 182 George Street, Providence RI, 02912, USA*

(E-mail: d.fedosov@fz-juelich.de)

Abstract

Red blood cells (RBCs) infected by the Plasmodium falciparum (Pf-RBCs) parasite lose their membrane deformability and exhibit an enhanced cytoadherence to vascular endothelium and to other healthy and infected RBCs. Such changes in RBC properties may lead to severe disruptions of normal blood circulation due to vessel occlusions. Another important aspect of cytoadhesion in malaria concerns the invasion stage of RBCs by a parasite. In this process, a parasite has to be able to bind to a RBC membrane, potentially re-orient itself after initial binding, and penetrate the cell membrane.

Using numerical simulations, we investigate various cytoadhesion aspects in malaria disease. In particular, we study the adhesive dynamics of Pf-RBCs as a function of wall-shear-stress (WSS) and other relevant parameters. Several types of adhesive behavior are identified including firm adhesion, flipping dynamics, and slow slipping along the wall. The flipping dynamics of Pf-RBCs (see Fig. 1), in particular, observed in experiments appears to be due to the increased stiffness of infected cells and the presence of the solid parasite inside the RBC, which may cause an irregular adhesion behavior. Specifically, a transition from crawling dynamics to flipping behavior occurs at a Young's modulus of approximately three times larger than that of healthy RBCs. The simulated dynamics of Pf-RBCs is in excellent quantitative agreement with available microfluidic experiments and the simulations provide new insights about Pf-RBC adhesion.

We also investigate the adhesion of a Pf-parasite to RBC membrane in the pre-invasion stage. Parasite adhesion to the membrane leads to strong RBC deformations, which may aid in the re-orientation of parasite and make further cell invasion possible. Another potential mechanism for the parasite re-orientation is an adhesion gradient along the parasite body, which can be presumably regulated by the parasite itself. We will test several possible scenarios and discuss the potential mechanisms which may govern parasite re-orientation and thus, affect RBC invasion.

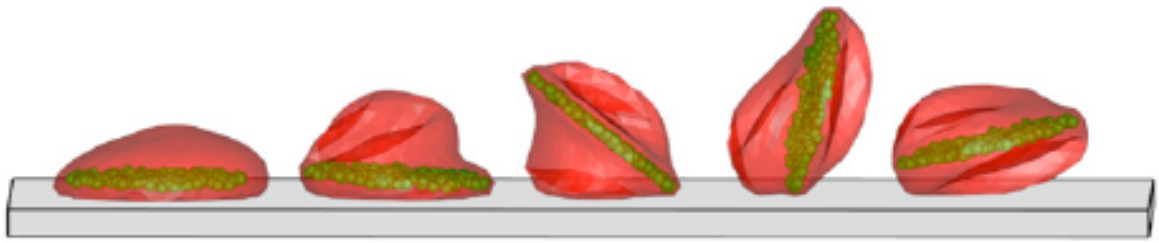

Figure 1: Side view of several snapshots of a rolling RBC with a parasite body inside the cell drawn in green. Coordinates along the wall for different snapshots are shifted to separate them for visual clarity. The RBC membrane is partially transparent.