Society of Engineering Science 51st Annual Technical Meeting

1–3 October 2014

Purdue University, West Lafayette, Indiana, USA

Molecular origins of the loss of deformability in *Plasmodium falciparum* infected erythrocytes: a coarse-grained modeling

Zhang, Yao, yuz137@psu.edu; Changjin Huang; Mahdi Golkaram; Sulin Zhang, Department of Engineering Science and Mechanics, The Pennsylvania State University, PA 16801, USA

ABSTRACT

Plasmodium falciparum, the most virulent human malaria parasite, invades human erythrocytes, exports proteins to modify erythrocyte membranes, endows erythrocyte with high stiffness and cytoadherence, and subsequently leading to blockage of blood vessels and dysfunction of organs. Despite continuous progress in experimental studies on erythrocyte remodeling triggered by *P. falciparum* infection, the underlying molecular mechanisms regarding how the microstructural modifications of erythrocyte membrane lead to the impressive loss of deformability remains elusive. Using a coarse-grained erythrocyte membrane model, capable of incorporating molecular level structural modifications caused by *P. falciparum*, we systematically investigated shear elasticity of the erythrocyte membranes. Our simulation results show that though the spectrin network accounts for the shear modulus of healthy erythrocyte, pure alteration of the spectrin network could not induce remarkable increase in the shear modulus. Instead, knob formation in the bilayer membrane significantly influences erythrocyte membrane via tightening the associations between spectrin network and lipid bilayer, thereby resulting in increased shear modulus and the loss of deformability. Evolution of knob density and size also plays an important role in enhancing the shear modulus. Shear moduli of *P. falciparum*-infected erythrocyte at different asexual stages obtained from our model are in good agreement with experimental results. Our findings offer molecular insights into the stiffening mechanism of *P. falciparum* infected erythrocytes.