**DIRECT NUMERICAL SIMULATION OF RED BLOOD CELL FLOW AND AGGREGATION**

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**Summary** The rheology of blood and its transport have physiological significance in blood circulation. The aggregation of red blood cells (RBC) plays a significant role in the rheology and flow characteristics of blood. Furthermore, RBC aggregation has clinical significance as it is used diagnostically to evaluate blood plasma concentration of certain macromolecules such as immunoglobulin and fibrogen (Reich, 1978 and Fung, 1997).

The aggregation of RBC is being studied using direct numerical simulation based on the lattice-Boltzmann (LB) computational approach (Aidun et al., 1998, Ding and Aidun 2003). The goal of our study is two fold. We aim to develop tools based on direct numerical simulation for analysis of blood flow including the RBC and other cells/particulate with all of the significant factors influencing the cell interaction and aggregation. We are also working on developing ‘universal’ scales and relations that can be used as predictive tools. Because of the high concentration of the RBC and the deformability of the membrane, a number of modifications are made to the LB method. Most significant is the capability to impose cell-cell and cell-wall interaction forces at the link-to-link level. The deformation of the cell membrane and the effects of surface charge and other surface properties can be added to the current method.

In the present simulations, the deformation of the membrane is neglected and the cell is treated as a solid object. Based on this approach, the dependency of the aggregate size on the shear rate and the RBC volume ratio is determined.

Aggregation of RBC has been considered by many investigators [5-13]. The aggregates may remain cylindrical or they may branch, forming network-like structures. For example, experiments on human erythrocytes show that not only rouleaux but also 3D aggregates develop. On the other hand, experiments on rat blood sample show that erythrocytes only form rouleaux in their own plasma without the development of 3D aggregates (Shiga et al, 1983). Other studies show significant differences in erythrocyte aggregate tendency between various animals and human (for example see Baskurt et al., 1997). The determinant factors for erythrocyte aggregation are complex and not well established. These include cell volume concentration, hydrodynamic effects, plasma proteins, surface charge and other surface phenomena.

When the size of the vessel is much larger than the size of the RBC, the membrane deformation may not be important. In these preliminary simulations, we neglect membrane deformation and only consider the hydrodynamic forces. The computational domain, as shown in Fig. 1, is a 3-D
cylinder with the total number of RBCs, N=265. Results of aggregate size distribution are show in Figure 2a. The distribution can be fitted by the power scaling relation given by 
\[ n(s) \propto \phi^{-\tau} \exp(-s/\Omega) \] with exponent \( \tau=2.5 \) and \( \Omega=9.23 \).

\[ \log[n(s)] = \log(\phi) - \tau \log(s) - \log(\Omega) \]

\[ n(s) = \phi^{-\theta} f(s/\phi^2) \]

Fig.2. (a) Simulation results for \( \phi=0.126, \text{Re}<<1 \) can be fitted by a scaling relation, as shown by the solid curve. (b) Simulation results for different volume concentration and slightly different Reynolds numbers (\( \square \): \( \phi=0.252 & \text{Re}<<1, +: \phi=0.126 & \text{Re}<<1, O: \phi=0.126 & \text{Re}=1.84 \) and \( \diamond \): \( \phi=0.063 & \text{Re}<<1 \)) and the finite-size-scaling relation (solid curve). See the text for details.

Results from direct simulations for different particle volume concentrations and slightly different Reynolds number are used to develop appropriate scaling relations for the aggregate size distribution. Cases with concentration ranging from \( \phi=0.252 \) to .063 and \( \text{Re}=1.84 \) and \( \text{Re}<<1 \) show that the exponential \( \tau \) in the scaling relation does not change while the values of \( \Omega \) changes in proportion to \( \phi^2 \). Then assuming 

\[ n(s) = \phi^{-\theta} f(s/\phi^2) \], we obtain \( n(s)\phi^5 = f(s/\phi^2) \), and \( f(x) = x^{-5/2} \exp(a-bx) \)

where \( a=5.20 \) and \( b=0.0022 \). The simulation results and the finite-size-scaling relation are shown in Figure 2b.

The duration for size distribution to approach to the final scaling relation in the lattice-Boltzmann simulation is very short; only about 0.1 seconds. In fact, in the first 4000 time steps the size distribution is already quite close to the equilibrium distribution. The results suggest that the hydrodynamic effects are more responsible for the first stage of the aggregation formation where other interactions we have not included in the simulation, such as the bridging by plasma proteins, and the influence of glyocalyx on RBC motion, might be more important in a longer time scale.

The main result in this simulation is the universal scaling relation for the aggregate size distribution. This scaling relation can be completed by adding the other important factors such as membrane deformation, protein links, and surface charge and other phenomena that have not been considered in this study.