# SEGREGATION PHENOMENA IN FLOWING SUSPENSIONS OF DEFORMABLE PARTICLES: TOWARD AN UNDERSTANDING OF CELL AND PARTICLE DYNAMICS IN BLOOD FLOW

Amit Kumar*, Kushal Sinha*, Rafael Henriquez Rivera* and Michael D. Graham*[a)]
*Department of Chemical and Biological Engineering, University of Wisconsin-Madison, Madison, Wisconsin 53706 USA

*Summary* Spatial segregation in the wall-normal direction during pressure-driven flow of suspensions containing a binary mixture of Neo-Hookean capsules with unequal membrane stiffnesses is investigated, using direct simulations. The study reveals that segregation is largely determined by the nature of pair collisions between different types of particles during flow. This knowledge will lead to a better understanding of the origins and consequences of segregation phenomena in blood flow.

## INTRODUCTION

Flowing suspensions of mixtures of particles with different rigidity are naturally encountered in blood flow. Blood is primarily a suspension of red blood cells (RBCs) with small amounts of white blood cells (WBCs) and platelets. The leukocytes and platelets are typically found in enhanced concentration near blood-vessel walls – this property is commonly known as margination and is critical for the physiological responses of inflammation and hemostasis [1, 2]. It is believed that the rigidity of the leukocytes and platelets play an important role in this margination phenomena. In contrast to the benefits arising from the stiff nature of the leukocytes and platelets, the stiffening of RBCs in various diseased states like malaria [3] and sickle cell disease [4] leads to various deleterious effects. Recently, there has also been a particular emphasis on drug delivery with particles via the bloodstream. A common target of such particles is the vascular walls [5], so in this context an ideal drug delivery particle must have an inherent propensity to segregate toward the walls. As such the design of an efficient drug delivery particle (via shape, size, and deformability) is an interesting problem in itself. Furthermore, the segregation properties of leukocytes, platelets, and infected RBCs can also be employed for their separation or detection in biomimetic microfluidic devices[6, 7, 8].

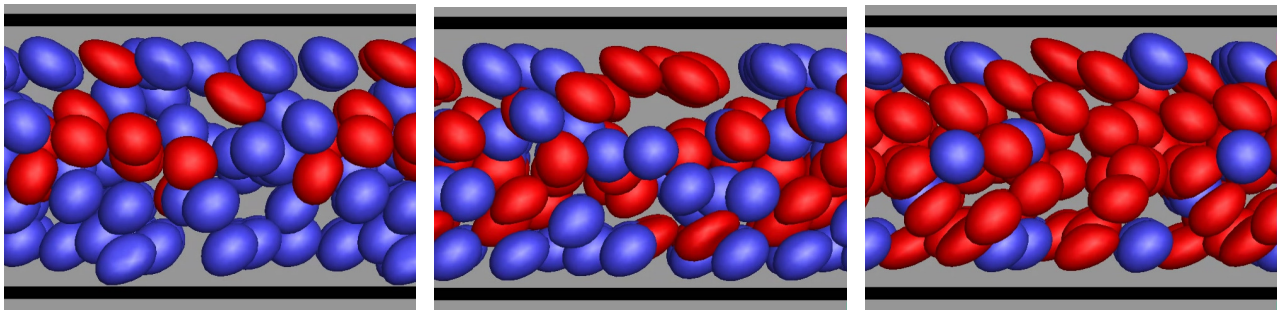
## FORMULATION

The discussion above clearly establishes the importance of rigidity based flow induced segregation in mixtures of particles. At the same time, it is also obvious that this phenomena is very poorly understood. The experimental observations of segregation phenomena involve a number of parameters (size, shape, deformability), and well-controlled studies that focus on changing only one property, for example the stiffness of the particles, are lacking in the literature. In the present effort, we seek to delineate the effect of rigidity on flow induced segregation by focusing on binary mixtures of deformable fluid-filled elastic capsules with unequal rigidities, but with identical size and spherical rest shape. The flow problem is investigated numerically using an accelerated implementation of the boundary integral method[9]. The specific system considered here is pressure driven flow in a planar slit[10]. The deformability of a capsule is expressed nondimensionally by the capillary number $\mathrm{Ca} = \mu\dot{\gamma}_w a/G_s$, where $\mu$ is the viscosity of the suspending and internal fluids, $\dot{\gamma}_w$ is the wall shear rate, $a$ is the equilibrium radius of a capsule and $G_s$. Since we study suspensions of binary mixtures of capsules with different rigidity, we remark that in a given flow, the values of $\mathrm{Ca}$ of the different particles are not equal: particles with the lower $G_s$ have a higher $\mathrm{Ca}$ and are termed floppy particles, while particles with the higher $G_s$ have a lower $\mathrm{Ca}$ and are termed stiff particles. Here the ratio of the moduli is 2.5. Another important parameter characterizing a binary mixture is the number fraction of one of species in the suspension – in this work, we employ the number fraction of the floppy particles $X_f$. The number fraction of the stiff particles can be obtained from $X_f$ as: $X_s = 1 - X_f$. The suspension as a whole is characterized by its volume fraction $\phi$.

## RESULTS AND DISCUSSION

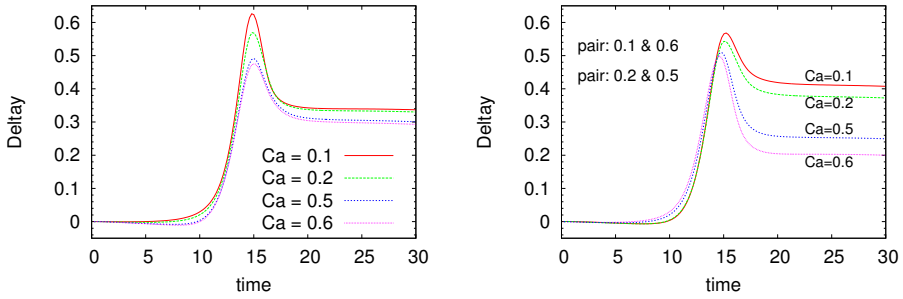
The detailed simulation results, illustrated in Figure 1, indicate two key observations: (i) with increasing fraction of floppy particles in the suspension, the stiff particles get increasingly localized in the near wall region, and (ii) with increasing fraction of stiff particles in the suspension, the floppy particles are increasingly depleted in the near wall region. As a result of this behavior, stiff particles segregate in the near wall region in a suspension of primarily floppy particles, while floppy particles segregate around the centerline in a suspension of primarily stiff particles. The degree of localization of stiff and floppy particles in the near wall region as a function of the fraction of the other particle type is found to be closely related to the cross-stream displacement of that species in heterogenous pair collisions, i.e. collisions involving a stiff and a floppy particle. In particular, in heterogenous pair collisions, the stiff particle undergoes much larger cross-stream displacement than the floppy particle as shown in Figure 2. As a result, a stiff particle in the near wall region gets increasingly localized as the fraction of floppy particles in the suspension increases, while the reverse is true for a floppy particle in the near wall region as the fraction of stiff particles in the suspension increases. All these observations can be

[a)] Corresponding author. E-mail: graham@engr.wisc.edu.



(a) $X_f = 0.2$ (b) $X_f = 0.5$ (c) $X_f = 0.8$

**Figure 1.** Simulation snapshots in the shear plane $(x - y)$ at $\phi = 0.2$ for different values of $X_f$. The snapshots show approximately 1.5 times the length of the simulation box in the $x$ direction. The stiffer particles ($\mathrm{Ca} = 0.2$) are shown in blue, while the floppy particles ($\mathrm{Ca} = 0.5$) are shown in red. Flow is left to right.




(a) homogeneous (b) heterogeneous

**Figure 2.** Pair collisions of isolated particles in shear: Displacement of particles relative to their initial position $(y - y_i)$ with time in (a) homogeneous pair collisions, (b) heterogeneous pair collisions, for pairs with capillary numbers $0.1$ and $0.6$ and pairs with capillary numbers $0.2$ and $0.5$.

successfully explained with a unified mechanism that incorporates the wall-induced migration of deformable suspended particles away from the wall and the particle fluxes associated with heterogeneous and homogeneous pair collisions.

These results show that by isolating the effect of differing rigidities in suspensions of otherwise identical particles, a key mechanism of the segregation that is widely observed in multicomponent suspensions can be identified. Having in hand an understanding of this mechanism now allows more rational approaches to development of quantitative models of segregation phenomena and processes that exploit them. This knowledge will also lead to a better understanding of the consequences of these phenomena in physiology and medicine.

This work is supported by NSF grants CBET-0852976 (funded under the American Recovery and Reinvestment Act of 2009) and CBET-1132579.

## References

[1] W. Tilles and E. C. Eckstein, "The near-wall excess of platelet-sized particles in blood flow: its dependence on hematocrit and wall shear rate," Microvascular Research **33,** 211–223 (1987).

[2] A. Jain and L. L. Munn, "Blood Cell Interactions and Segregation in Flow," PLos ONE **4,** e7104 (2009).

[3] R. Suwanarusk, B. M. Cooke, A. M. Dondorp, K. Silamut, J. Sattabongkot, N. J. White, and R. Udomsangpetch, "The Deformability of Red Blood Cells Parasitized by Plasmodium falciparum and P. vivax," The Journal of Infectious Diseases **189,** 190–194 (2004).

[4] H. F. Bunn, "Pathogenesis and treatment of sickle cell disease," The New England Journal of Medicine **337,** 762–769 (1997).

[5] R. B. Huang, S. Mocherla, M. J. Heslinga, P. Charoenphol, and O. Eniola-Adefeso, "Dynamic and cellular interactions of nanoparticles in vascular-targeted drug delivery," Molecular Membrane Biology **27,** 312–327 (2010).

[6] S. S. Shevkoplyas, T. Yoshida, L. L. Munn, and M. W. Bitensky, "Biomimetic Autoseparation of Leukocytes from Whole Blood in a Microfluidic Device," Analytical Chemistry **77,** 933–937 (2005).

[7] P. Sethu, A. Sin, and M. Toner, "Microfluidic diffusive filter for apheresis (leukapheresis)," Lab Chip **6,** 83–89 (2006).

[8] H. W. Hou, A. A. S. Bhagat, A. G. L. Chong, P. Mao, K. S. W. Tan, J. Han, and C. T. Lim, "Deformability based cell margination–A simple microfluidic design for malaria-infected erythrocyte separation," Lab Chip **10,** 2605–2613 (2010).

[9] A. Kumar and M. D. Graham, "Accelerated boundary integral method for multiphase flow in non-periodic geometries," (2011), submitted, eprint arXiv:1109.6587.

[10] A. Kumar and M. D. Graham, "Segregation by membrane rigidity in flowing binary suspensions of elastic capsules," Physical Review E 84 (2011).