Letter to the Editor

Hydrodynamic Recruitment of Rolling Leukocytes In Vitro

Recently, Zhang and Neelamegham (2002) argue that the hydrodynamic recruitment of rolling leukocytes, as predicted theoretically and observed experimentally by King and Hammer (2001a), occurs over longer distances than that attributable to the disturbance caused by a rigid spherical cell in shear flow (4–5 cell diameters versus 2.5 cell diameters). Their argument is based on an *approximate* calculation of the flow around a sphere, neglecting both the disturbance caused by the wall and the disturbance caused by the second (freestream) cell. Zhang and Neelamegham provide supplemental data (http://www.end.buffalo.edu/~neel/pplate.html) that suggest that cell-cell hydrodynamic (i.e., nonadhesive) interactions may not affect the tethering flux or cell rolling velocity. We would like to clarify that such an experiment does not address the issue of hydrodynamic recruitment as defined by King and Hammer. Additionally, we point out that the supplemental data of Zhang and Neelamegham do contain an observation that reveals that hydrodynamic recruitment is indeed an important mechanism in in vitro flow assays.

Hydrodynamic recruitment, as described by King and Hammer (2001a), refers to the phenomenon that the collision between a freestream cell and a previously adherent cell can result in recruitment of the freestream cell to the wall through long-range hydrodynamic interactions. Our model includes the hydrodynamic effect of the wall, as well as the effect of both spheres involved in the binary collision. Hydrodynamic recruitment has been verified both in detailed numerical simulations (King and Hammer, 2001b) and in a cell-free flow chamber assay using sialyl Lewis$^{\times}$-coated beads tethering on a P-selectin surface. We showed that this is due to a slight vertical motion (i.e., normal to the plane) of the freestream cell that is induced by hydrodynamic interaction with the adherent cell on the surface. Over a wide range of initial positions and physical parameter values, we have found the normal motion of the freestream cell to exhibit a local minimum in separation from the wall at around 4–5 cell diameters either upstream or downstream of the adherent particle. The enhanced probability for adhesion between the freestream cell and the wall is due to this motion of bringing the surface of the freestream cell closer to the reactive wall by ~10–100 nm, and not due to the slight reduction in the local shear rate caused by the presence of the adherent cell. The maximum interaction distance of 2.5 cell diameters calculated by Zhang and Neelamegham (2002) is rather arbitrarily derived as the distance at which the local reduction of the shear rate has attenuated to 5%. An important requirement in the hydrodynamic recruitment mechanism is that the freestream cell be capable of being recruited—that both cells in the collision present the proper surface chemistry to bind to the reactive wall. Collisions with inert cells are not expected to enhance overall tethering frequencies, since an inert cell cannot bind the surface despite being pulled toward it through hydrodynamic interactions.

Zhang and Neelamegham (2002) present the results of a set of experiments to examine the effect of "nonadhesive interactions" on the adherent cell density in a parallel plate flow chamber, as supplemental material (http://www.end.buffalo.edu/~neel/pplate.html). Based on the observation that adding nonadhesive cells does not significantly increase the adherent cell density, Zhang and Neelamegham argue that hydrodynamic recruitment does not occur in their system. Of course, such an experiment does not probe into the hydrodynamic recruitment mechanism described by King and Hammer (2001a), since a nonadhesive cell cannot be recruited to the surface despite interacting hydrodynamically with the adherent cell. Their supplementary Figure 1S does contain an interesting observation, however. When increasing the concentration of adhesive cells in their system from 0.07×10^6 to 0.2×10^6 cells/ml, Zhang and Neelamegham measured an increase in adherent cell density from 2.5×10^3 to 1.4×10^4 cells/cm^2. Thus, a threefold increase in cell concentration results in a nearly sixfold increase in tethering frequency. Such a superlinear dependence on cell concentration suggests an interactive cell-cell enhancement to tethering frequency such as the hydrodynamic recruitment mechanism described by King and Hammer, occurring even at very low densities.

REFERENCES

King, M. R., and D. A. Hammer. 2001a. Multiparticle adhesive dynamics: hydrodynamic recruitment of rolling leukocytes. *Proc. Natl. Acad. Sci. USA.* 98:14919–14924.

King, M. R., and D. A. Hammer. 2001b. Multiparticle adhesive dynamics. Interactions between stably rolling cells. *Biophys. J.* 81:799–813.

Zhang, Y., and S. Neelamegham. 2002. Estimating the efficiency of cell capture and arrest in flow chambers: Study of neutrophil binding via E-selectin and ICAM-1. *Biophys. J.* 83:1934–1952.

Michael R. King* and Daniel A. Hammer†

**Department of Biomedical Engineering*
University of Rochester
Rochester, NY, USA

†Department of Bioengineering
University of Pennsylvania
Philadelphia, PA, USA

Submitted December 17, 2002, and accepted for publication January 21, 2003.

0006-3495/03/06/4182/01 $2.00