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The effect of shape on the margination dynamics of non-neutrally buoyant particles in two-dimensional shear flows

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Abstract

The margination dynamics of microparticles with different shapes has been analyzed within a laminar flow mimicking the hydrodynamic conditions in the microcirculation. Silica spherical particles, quasi-hemispherical and discoidal silicon particles have been perfused in a parallel plate flow chamber. The effect of the shape and density on their margination propensity has been investigated at different physiologically relevant shear rates S. Simple scaling laws have been derived showing that the number n of marginating particles scales as $S^{-0.63}$ for the spheres; $S^{-0.85}$ for discoidal and S^{-1} for quasi-hemispherical particles, regardless of their density and size. Within the range considered for the shear rate, discoidal particles marginate in a larger number compared to quasi-hemispherical and spherical particles. These results may be of interest in drug delivery and bio-imaging applications, where particles are expected to drift towards and interact with the walls of the blood vessels.

Keywords: Particle dynamics; Sedimentation; Fluidic chamber; Drug delivery

1. Introduction

The intravascular delivery of nanoparticles for biomedical imaging and therapy is being recognized as a powerful and promising tool in cardiovascular and oncological applications (LaVan et al., 2003; Ferrari, 2005a, b). Nanoparticles can be loaded with drug molecules and contrast agents and transported by the blood flow through the circulatory system. They are generally decorated with ligand molecules which are able to interact specifically with antigens expressed over diseased cells (target cells), which could be cells lining the blood vessels (vascular targeting) or cells in the extravascular space.

The power of nanoparticles over freely administrated drug molecules or imaging tracers relies on their multifunctionality and engineerability. As regarding multifunctionality, a nanoparticle can carry several hundreds of thousands of drug molecules and imaging agents increasing dramatically the drug dose released locally over time and the imaging contrast too. Different drug molecules can be loaded and released with a precise time schedule at the same location allowing for complex multidrug therapies. But even more important than multifunctionality is the engineerability of the nanoparticles. In fact, differently from drug molecules, nanoparticles are entities with defined geometrical, physical and chemical properties which can be controlled during the fabrication and

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synthesis process and provide superior particle performances (Decuzzi and Ferrari, 2006). Several different particles have been presented in the literature that may be used for both therapy and medical imaging, ranging in size from few tens of nanometers to hundreds of nanometers (Choi et al., 2005; Duncan, 2003; Crommelin and Schreier, 1994) and up to few microns (Cohen et al., 2003); with different shapes, from the classical sphere, to spheroids (van Dillen et al., 2004) and even more complex shapes (Rolland et al., 2005) and with different composition and chemico-physical properties.

An 'optimally' designed nanoparticle should be able to navigate into the circulatory system, recognize the diseased cells (biological target) with high selectivity and adhere firmly to them (Decuzzi and Ferrari, 2006). The recognition process not only relies on the specific and non-specific interactions originating at the particle/cell interface, but evidently requires also close proximity between the particle and the target cell. In other words, particles should be designed to drift laterally towards the vessel walls, as leukocytes during an inflammatory process, rather than moving within the core of the vessels, as red blood cells generally do in the macro- and micro-circulation. By doing so, a particle would have the ability of sensing the vessel walls for biological and biophysical diversities, such as the overexpression of specific antigens (Neri and Bicknell, 2005) which could be used as 'docking site' in vascular targeting, or the presence of openings and fenestrations (di Tomaso et al., 2005) through which sufficiently small particles can cross the endothelial barrier.

The margination of leukocytes, at sites of inflammation, is an active process accompanied by a localized dilatation of the vessels and a decrease in blood flow velocity, and possibly favored by the interaction with the red blood cells which accumulating within the core of the vessels tend to push the leukocytes towards the periphery (Goldsmith and Spain, 1984). Nanoparticles used in biomedical applications are at least one order of magnitude smaller than red blood cells and leukocytes, therefore their margination cannot rely on such a mechanism. The shape and the density of the particles can be tailored to affect their margination propensity: spherical particles in a capillary flow would drift towards the vessel walls if and only if they are subjected to an external force field (Decuzzi et al., 2005); non-neutrally bouyant spherical particles have been observed and are predicted to drift laterally both in horizontal and vertical capillaries (see Hogg, 1994 and references there in); non-spherical particles exhibit a fairly complex dynamics with tumbling and rolling motions (Gavze and Shapiro, 1998; Pozrikidis, 2006). In this paper, the margination dynamics of non-neutrally buoyant particles with different shapes (quasi-hemispherical and discoidal) within a capillary flow is studied and compared to the dynamics of classical spherical particles.

2. Materials and methods

2.1. The particles

The spherical particles were purchased from polysciences. They are uniform, plain non-porous silica (SiO_2) microspheres with a diameter of about 1 μm and a density $\rho = 2000\,kg/m^3$, as shown by the SEM image in Fig. 1. The solid polysilicon particles were fabricated starting with a cleaned silicon wafer. Then an 800 nm silicon dioxide film was deposited by using wet oxidation process; a 330 nm polysilicon film was deposited by LPCVD. Finally, the 1.5 μm circular particles were patterned all over the polysilicon film using a standard photolithography process. Reactive ion etching was applied to remove undesired areas, and after stripping the photoresist, the polysilicon particles were released by removing the silicon dioxide layer in HF solution. An SEM image of the particle is given in Fig. 1. The quasi-hemispherical particles are porous silicon particles with different diameters and densities ($\simeq$ 1400 and 1900 kg/m^3), obtained by controlling particle porosity during the manufacturing process. Heavily doped 4 in p++ type (1 0 0) wafer were made into porous silicon particles modifying the protocols described in Cohen et al. (2003) to attain extreme control over the key characteristics of the microparticles such as shape and pore morphology. High uniformity and reproducibility were observed through SEM micrographs of the particles taken over different wafers (Fig. 1). The larger particles were estimated having a 3.2 ± 0.1 μm diameter and 1.05 μm thickness while the smaller were estimated having a diameter 1.6 ± 0.1 μm and 0.86 μm thickness. The microparticles were oxidized to obtain a high degree of hydrophilicity.

2.2. The flow chamber system

The system is similar to that used by several groups for analyzing the dynamics of circulating blood cells (among many others Gopalan et al., 1997) and microparticles (Shinde Patil et al., 2001). It consists of a PMMA flow deck with inlet and outlet bores, a silicon rubber gasket and a 35 mm glass dish sandwiched together (Fig. 2) from GlycoTech Corporation. The channel, defined by the gasket, has a thickness h of 0.01 in (254 μm), a

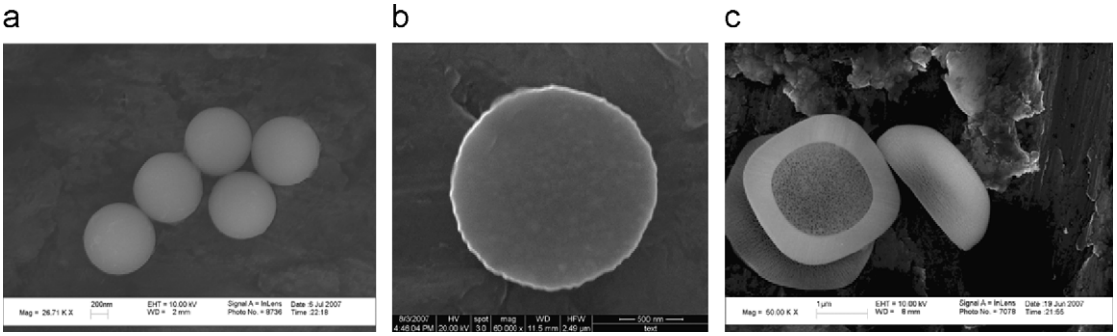

Fig. 1. SEM micrographs of spherical silica particles (1 μm solid particle), of discoidal polysilicon particles (1.5 μm × 0.3 μm solid particle), and of quasi-hemispherical silicon particles (3.2 μm porous particle).