Hydrodynamic Focusing Effect on Two-Unmixed-Fluid in Microchannels
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Micro-flow focusing

Manipulation of liquid and gas flows in microchannels has been a central technology in a number of microfluidic systems that are being developed for chemical, biological, medical applications, and fundamental researches. Particularly, micro-flow focusing technique provides an effective means of controlling the passage of chemical reagent or bio-samples through microfluidic channels. Fig. 1 schematically illustrates the flow focusing in cross-form microchannels. Two neighboring sheath flows are used to constrain the central sample flow laterally (horizontally) within the center of the microchannel. Hydrodynamic forces provide a convenient means of adjusting the focused (center) stream width by regulating the relative volumetric flow rates of the inlet streams. Typically, the hydrodynamic flow focusing techniques employed in the applications above can be classified as either: (i) multi-phase flow focusing (i.e. liquid-liquid or liquid-gas) [1] or (ii) liquid single-phase flow focusing [2]. Recently, hydrodynamic focusing have been successfully demonstrated in a wide variety of microfluidic applications, including in micro-flow cytometers for cells/particles counting and sorting [3], rapid diffusion-based micro-mixers for the kinetic studies of protein folding, microfluidic optical waveguides [4] and fluorescent light sources, micro-droplet and bubble generators [1], micro- and nano-particles productions and cell encapsulations etc.

FIG. 1 Schematic illustration of flow focusing in cross-form microchannels.

Hydrodynamic focusing effect on two-immiscible-fluid parallel flow
The purpose of the current study is to develop a theoretical model to predict the width of a hydrodynamically focused stream (or equivalently, the position of the side stream-center stream interface) in two-immiscible-fluid parallel flow as a function of the flow rate ratio, the viscosity ratio of the two fluids, and the aspect ratio of the microchannel. In developing a theoretical model to predict the width of the hydrodynamically focused stream (or equivalently, the position of the side stream-center stream interface), this study makes the following assumptions:

i. The flow focusing system is stable, and hence parallel flow is maintained in the outlet channel.
ii. The interface between the immiscible fluid flows is planar, i.e. the contact angle between the two streams is close to 90°.
iii. The fluids are Newtonian.
iv. The flow is laminar, steady state and fully-developed.

Using the method of separation variables to solve the governing equation of this flow system, the focused stream width or the position of two-fluid interface can be expressed as: $W = w_2/w = f(\alpha, \gamma, \epsilon)$, where $\alpha$ is the side stream to center stream flow rate ratio, $\gamma$ is the viscosity ratio of the two fluids, and $\epsilon$ is the aspect ratio of the microchannels. In the limiting case, i.e. $\epsilon << 1$, the focused stream width or the position of two-fluid interface can be simplified to the form: $W_2 = \gamma/(\gamma + \alpha)$.

![FIG. 2 Velocity profiles associated with different fluid viscosity ratios ($\gamma$) in microchannels when the channel aspect ratio $\epsilon = 0.1$. (a) $\gamma = 0.1$ and (b) $\gamma = 10$.](image)

Figure 2 presents the dimensionless velocity profiles for the different fluid viscosity ratios ($\gamma = 0.1$ and 10) when the channel aspect ratio $\epsilon = 0.1$. The figures show that the average flow velocity of the center stream is higher than that of the side streams when the viscosity of the side stream fluid is greater than that of the center stream fluid (i.e. the viscosity ratio is less than unity). However, when the viscosity of the center stream fluid is greater than that of the side stream fluid (i.e. $\gamma = 10$), the average velocity of the center stream is lower than that of the side streams. Fig. 3(a) presents the theoretical relationship between the focused stream width and the flow rate ratio as a function of the viscosity when the channel aspect ratio $\epsilon = 0.1$. For a constant flow rate ratio, the focused stream width increases as the viscosity ratio increases. This phenomenon is the result of the uniform pressure drop across the outlet channel, which causes the average velocity of the more viscous fluid to be lower than that of the less viscous fluid (see Fig. 2). In order to achieve the required flow rate, the more viscous fluid stream must therefore spread...
over a broader width. This phenomenon is known as “hydrodynamic spreading”. To maintain the interface at a fixed position (e.g. $W_2=0.5$) for different viscosity ratios, the flow rate ratio of the two fluids must be adjusted. Furthermore, it can be seen that the focused stream width decreases as the flow rate ratio is increased for any viscosity ratio. But the focused stream width varies insignificantly with the flow rate ratio when the viscosity ratio is large (i.e. the center stream is more viscous).

![Figure 3](image)

**FIG. 3**(a) Variation of dimensionless half-width of focused stream with flow rate ratio as function of viscosity ratio for constant aspect ratio of $\varepsilon=0.1$. (b) Variation of dimensionless half-width of focused stream with viscosity ratio for constant flow rate ratio of $\alpha=1.0$ and microchannel aspect ratio of $\varepsilon=0.1$.

**Microfluidic viscosimeter**

Figure 3(b) illustrates the relationship between the focused stream width and the viscosity ratio for a constant flow rate ratio of $\alpha=1.0$. The figure shows that if the viscosity of one of the two fluids is known, the viscosity of the second fluid can be derived by measuring the width of the focused stream. In other words, the microfluidic device can function as a microfluidic viscometer. When the channel is very thin (i.e. $\varepsilon<<1$) and the flow rate ratio is unity, the focused stream width or the position of two-fluid interface can be simplified to the form: $W_2 = \mu_2/(\mu_1 + \mu_2)$. If $\mu_1$ and $W_2$ are known, the viscosity of the second fluid can be calculated from the expression: $\mu_2 = \mu_1 W_2/(1-W_2)$.

**References**

Synthesis of Water-Soluble Blue Photoluminescent Silicon Nanocrystals with Oxide Surface Passivation
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Semiconductor nanocrystals are receiving widespread interests owing to their excellent efficiency of light emission and many promising applications in biological fluorescence imaging and optoelectronic devices. Many efforts have been made on the utilization of CdSe-ZnS core-shell nanocrystals because of their high luminous efficiency and tunable emission light in visible region. However, the potential toxicology problems arisen from Cd may limit their utilization. Silicon (Si) is an essential material for optoelectronic application with low toxicity. Although it has an indirect band gap in the bulk form showing a low photoluminescence (PL) yield in near IR, an enhanced PL efficiency along with a shift towards the visible region could be achieved by decreasing its size to the order of or less than the bulk exciton Bohr radius of 4 nm because of the quantum confinement in Si nanocrystals.

A number of methods have been used for the synthesis of Si nanocrystals. Additional surface treatments are required to enhance the PL stability and dispersibility in different media. Noteworthily, the oxidation on the surface might lead to good dispersibility in water because of the hydrophilicity of silicon oxide. However, the Si nanocrystals with an oxide surface shell are theoretically predicted to exhibit a yellow-red emission with a long radiative lifetime (10^{-3} – 10^{-6} s). The slow recombination rate limits their use in biological imaging.

In this paper, we report a facile method to synthesize the Si nanocrystals with oxide surface passivation. Generally, Br_2 was added to anhydrous n-octane containing Mg_2Si powder. The mixture was stirred vigorously for 24 h at room temperature and then heated slowly to 125 °C with a reflux. After heating for 60 h, the mixture was cooled to room temperature. The mixture was centrifuged and then vacuum dried to remove the solvent. The surface hydrophilic treatment was performed by adding 1-butanol to the as-synthesized Si nanocrystals and stirring the mixture at room temperature for 36 h. The solvent was then removed and 1 M HCl was added. The mixture was stirred for a few minutes and then two phases were formed upon the addition of hexane. Finally, the Si nanocrystals from the upper hexane solution were collected and then re-dispersed in water after vacuum drying.

TEM analysis (Fig. 1a) revealed the resultant Si nanocrystals were nearly spherical and discrete completely with a mean diameter of 4.11 nm. This
size was close to the bulk exciton Bohr radius and about 50% of Si nanocrystals were larger than 4 nm, implying their optical property would be determined not only by the radiative recombination via the direct band gap transitions but also by the indirect band gap transitions. The high-resolution TEM (HRTEM) image (Fig. 1b) indicated they had a highly crystallinity and the lattice spacings of 0.32 nm was related to the (111) plane of diamond structured silicon. Also, the nanocrystal seemed to be covered by an amorphous (or low crystalline) nanoshell (less than 1 nm), implying the formation of surface oxide. In addition, the selected-area electron diffraction (SAED) pattern indicated three diffraction rings corresponding to the (111), (220), and (311) planes of diamond structured silicon. The XRD pattern also showed three characteristic peaks for the (111), (220), and (311) planes of diamond structured silicon at $\theta = 28.47, 47.34, \text{and } 56.17^\circ$. These results demonstrated that the resultant Si nanocrystals had a diamond structure.

EDX spectrum (Fig. 2a) showed the peaks for Si, O, C, and Cu, confirming the presence of Si in the nanocrystals. The presence of C and Cu should be originated from the carbon-coated copper grid used for analysis. As for O, it might be resulted by the surface oxidation. To realize the surface state, we examined the FTIR spectrum (Fig. 2b). The characteristic peaks due to Si-O-Si stretch vibration were clearly observed at 1100 and 804 cm$^{-1}$, revealing the formation of silicon oxide shell. As for the peaks at 1630 and 3400 cm$^{-1}$, they might be attributed to the OH bending and stretching modes, respectively, for silicon oxide. Moreover, we also conducted the XPS analysis. The wide scan XPS spectrum (Fig. 3a) indicated the O peaks. The Si$_{2p}$ core-level spectrum (Fig. 3b) also indicated the distinct Si$_{2p}$ signal at 103.3 eV due to Si in SiO$_2$ in addition to the peak at about 99.5 eV for Si, was also observed. So the oxidation on the particle surface could be demonstrated.
Fig. 3. XPS wide scan spectrum (a) and Si$_{2p}$ core-level spectrum (b) of oxide-passivated Si nanocrystals.

Fig. 4. (a) UV-VIS absorption spectrum of oxide-passivated Si nanocrystals in water. (b) PL spectra of oxide-passivated Si nanocrystals in water at room temperature with various excitation wavelengths. The bottom left inset shows a fluorescence image for the aqueous solution of oxide-passivated Si nanocrystals when excited with a UV lamp. (c) Time-resolved PL spectra of oxide-passivated Si nanocrystals for various time intervals. The emission was monitored at 480nm using an excitation wavelength of 375nm. (d) PL spectra of oxide-passivated Si nanocrystals in water at room temperature for various time intervals with an excitation wavelength of 350nm.
The resultant Si nanocrystals exhibited good dispersibility in water due to the hydrophilicity of surface oxide. Their UV-VIS absorption spectrum in water (Fig. 4a) indicated a gradual increase in the absorbance with decreasing the wavelength from the on-set wavelength of 450 nm (related to the absorption edge of 2.75 eV), which is characteristic of absorption across the indirect band gap. Moreover, the absorption spectrum showed a rather weak feature at about 260 nm, which could be attributed to the $\Gamma$ - $\Gamma$ direct band gap transition. Such a large band gap (4.8 eV) was usually observed for 1-2 nm Si nanocrystals. Although the particle size distribution indicated only small part of Si nanocrystals were in this range, actually more Si nanocrystals might have core diameters in this range after subtracting their oxide layer. So the absorption at about 260 nm might be referred to the Si nanocrystals with core diameters less than 2 nm.

Fig. 4b shows the PL spectra of the oxide-passivated Si nanocrystals in water at room temperature with excitation wavelengths ranging from 340 to 370 nm. The maximum emission peak was centered at about 460 nm while using an excitation wavelength of 350 nm. The monotonic shift of emission wavelength with the excitation wavelength could be attributed to the excitation of different sizes of Si nanocrystals, reflecting the particle size distribution. In addition, the bottom left inset in Fig. 4b shows the fluorescence image for the oxide-passivated Si nanocrystals in water when excited with a UV lamp. Obviously, a homogeneous dispersion system was obtained and UV excitation led to the bright blue fluorescence, revealing that water-soluble blue PL Si nanocrystals have been synthesized.

PL was affected by both the particle size and surface. The diameter of Si nanocrystals for the blue emission via the direct electron-hole recombination across the $\Gamma$ - $\Gamma$ direct band gap should be below about 2 nm. In this work, only a part of oxide-passivated Si nanocrystals were in this range even if subtracting the oxide layer. So the particle surface must play a key role in the blue emission, particularly for those with core diameters larger than 2 nm. It was suggested that some oxide-related defects might be formed within the surface oxide layer of Si nanocrystals which might act as the radiative centers for the recombination of electron-hole pairs (generated in Si nanocrystals) to result in the blue emission.

To further understand the PL property, the time-resolved PL spectrum of the resultant Si nanocrystals in water was measured by monitoring the emission at 480 nm using an excitation wavelength of 375 nm. As shown in Fig. 4c, the PL decays after immersion in water for 1 day and 1 month were almost the same, revealing the high stability in water. The PL decay required a three exponential fit with time constants of 0.60, 2.73, and 8.86 ns, suggesting that there exist multiple de-excitation process in the Si nanocrystals. Such a rapid decay with an overall average decay of 4.06 ns implied that, for the oxide-passivated Si nanocrystals synthesized in this work, the recombination of electron-hole pairs via the surface oxide-related radiative centers might be as rapid as that across the $\Gamma$ - $\Gamma$ direct band gap.

Fig. 4d shows the PL spectra of the oxide-passivated Si nanocrystals in water at various time intervals. They displayed a similar curve feature. After immersion in water for 6 months, about 95% of the initial maximum intensity was maintained and only a slight red shift (8 nm) was observed. The presence of Si=O bonds and Si-O-Si bridge bonds at the surface can affect the electronic behavior of Si clusters. The energy gap will be reduced, leading a red shift. In this study, more Si=O bonds and Si-O-Si bridge bonds might be introduced at the surface after immersion in water for 6 months. Although the Si cores became smaller, the new oxygen-related states localized in the band gap might partially overwhelm the contribution from the quantum confinement effect which led to a blue shift. Thus, the oxidation was not serious enough to cause the significant change in the bright blue fluorescence.
The quantum yield of the oxide-passivated Si nanocrystals was estimated from its PL spectrum using Coumarin 102 as a standard according to the comparative method with an excitation wavelength of 380 nm. The quantum yield for the sample immersion in water for 6 months was found to be as high as 12 % at the peak wavelength of 480 nm. This was slightly higher than the maximum value reported in the literature (10%).

In summary, water-soluble Si nanocrystals with oxide surface passivation were synthesized via a facile solution route. They exhibited good dispersibility and stability in water with a strong blue PL. Their size, structure, surface state, and optical properties have been well characterized. The solution route proposed was easy to operate and the resultant Si nanocrystals with oxide surface passivation may find promising applications in optoelectronic devices and biological labeling.
The phase-response effect of size-dependent optical enhancement in a single nanoparticle
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With the rapid advance of nanophotonics, the optical effects of metal nanoparticles, such as surface plasmonic resonance (SPR), surface enhanced Raman scattering (SERS), are always attractive for basic physics and a lot of applications. Here, we tried to analyze near-field phase-response in a single silver nanoparticle (NP), a pair of NP, and extending to nanostructure. It is well-known that optical properties of metal nanoparticles strongly depend on plasmon resonance modes, which can be tuned via controlling the particle’s size, shape and distance between each other [1]. The absorption/scattering cross-section of a particle expands significantly, contributing to the local electromagnetic (EM) field enhancement [2]. The effect of optical enhancement of nanoparticles has been studied in various experiments of surface-enhanced spectroscopy for a long time [3]. When the wavelength of incident light coincides with the wavelength of plasmon resonance, the absorption/scattering cross-section of a particle expands significantly [4]. The re-radiated electromagnetic (EM) field from the particle exhibits phase difference (\( \phi \)) relative to the incident EM field [5]. In this report, the plasmon-photon interaction is directly observed in the vicinity of silver nanoparticles through a near-field scanning optical microscope (NSOM). Our results manifest the correlation of phase-response and size-depend optical enhancement. Detailed interference behaviors between optical excitation and plasmon mediated re-radiation are revealed on a single particle basis. This observation facilitates nano-applications in controlling the spatial distribution of surface plasmon (SP) modes by means of nanostructures.

Such observation of SP phase response has been recently demonstrated in NSOM experiments on a single particle basis [6], but the SP phase dependency on particle size has not been well addressed. Through the study of size-/wavelength-dependent optical enhancement, we retrieved the phase shift of plasmonic re-radiation from the EM field distribution for each nanoparticle.
Fig. 1. (a) NSOM setup. (b) The absorption spectrum of Ag nanoparticles. The spectral positions of the NSOM excitations are shown with RGB lines. Inset: SEM image of Ag nanoparticles.

Figure 1(a) shows the scheme of experimental setup. Three lasers (a He-Ne laser ($\lambda$=633nm) and two solid-state lasers ($\lambda$=532 nm, 488 nm) were used. They were individually coupled into the probe as the light source for exciting Ag nanoparticles. A random distribution of Ag nanoparticles with different sizes was fabricated by a high-temperature annealing technique. The diameter ranges from 15 nm to 150 nm. Fig. 1(b) gives the far-field absorption spectrum of Ag nanoparticle film measured by a UV/VIS/NIR spectrometer.

Figure 2 shows the simulation results. The purpose of this theoretical simulation is to qualitatively analyze the far-field interference between the re-radiated field from the nanoparticles and the propagating field from the fiber tip. We follow the instruction by Choi et al [6].

Fig. 3 displays NSOM images of a single silver nanoparticle of 50-nm diameter. For this particle, the plasmon resonance wavelength is about 530 nm and thus significantly larger resonance enhancement is
provided by the 532-nm excitation. With the 633-nm excitation, though not at resonance, constructive interference exhibits between excitation and re-radiation, resulting in a weak, but positive signal. At 532 nm, which is on resonance, the particle dipolar re-radiation dominates, producing a stronger signal. But for the 488-nm excitation, the phase-shift of the polarizability resulted in a destructive interference, and thus a dip is observed. These results agree well with the simulations.

Fig. 3. Measured NSOM images of a 50-nm nanoparticle.

Fig. 4 outlines the particle size spectra of interfered optical far-field intensity with RGB excitations. The plasmon resonance peak of 633-nm excitation is located at the diameter of 75 nm, while that of 532-nm excitation is at 50 nm. The resonance peak of 488-nm excitation approaches its maximum toward a diameter of smaller than 40 nm. Ag nanoparticles with diameters larger than 75 nm can be employed to modulate the phase between $\pi/2$ and $\pi$. Those are smaller than 75 nm can be used to control the phase between 0 and $\pi$. Similarly, for the 532-nm excitation, the phase-modulation of $\pi/2$ is expected with 50-nm nanoparticles. These results validate the possibility of spatial manipulation of SP phases by modulating the size of metal nanoparticle or by selecting appropriate wavelengths.
Fig. 4. Particle size spectra for RGB excitations. The tendency of shorter wavelength resonant with smaller silver nanoparticles is evident.

In conclusion, our result manifests the correlation between plasmon resonance and the size of a single metal nanoparticle with the aid of a multiple-wavelength NSOM. We have shown that the size-/wavelength-dependent optical enhancement within a single silver nanoparticle can be revealed through isolated excitation. By visualizing the interference pattern between the plasmonic re-radiation and the excitation wave in the far field, the relative SP phase-shift across the resonant wavelength can be quantitatively extracted. The phase-response properties may be employed in allocating the spatial distribution of localized SP modes on a nanostructured surface.

REFERENCES:

Survivin, a novel therapeutic target for cardiac cell therapy, determines cardiac function by controlling total cardiomyocyte number

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The dominant cause of heart failure is regional loss of myocardium due to coronary artery disease. In the ischemic region, cardiomyocytes undergo necrosis, apoptosis and autophagy, and are not adequately replaced, leading to scar formation and ultimately, loss of ventricular function. Myocardial regeneration aims at protecting cardiomyocyte death and regrowing new cardiomyocytes to improve cardiac performance. However, this enthusiasm is frequently challenged by the fact that the mammalian heart, a terminally differentiated organ, is incapable of spontaneous regeneration.

Figure 1. Survivin overexpression prevents cardiomyocyte apoptosis and induces cell proliferation. A, Adenoviral overexpression of survivin (Ad-svv) or green fluorescence protein (Ad-GFP) in cardiomyocytes (CM) subjected to apoptosis induced by doxorubicin (Dox). B, DNA synthesis of cardiomyocytes. **, p<0.01.

Survivin is the smallest member of the inhibitor of apoptosis protein (IAP) family. Previous studies have shown that survivin is a key modulator of apoptosis inhibition and cell cycle progression in cancer cells. However, the function of survivin in the heart is largely unknown. In this work led by Professor Bodo Levkau (University of Essen, Germany), we showed evidence suggesting the potential of using survivin for cardiac regeneration. First we showed that transient overexpression of survivin induced cell cycle progression in cardiomyocytes. We found that in cultured neonatal cardiomyocytes, adenoviral
overexpression of survivin (Ad-SVV) protected cardiomyocytes from doxorubicin-induced apoptosis (by DNA fragmentation using flow cytometry) and increased DNA synthesis (by [3H]thymidine incorporation into DNA), compared with GFP overexpression (Ad-GFP) as control (Figure 1). To further confirm the pro-mitotic effect of survivin in cardiomyocytes, we examined cell cycle progression in cardiomyocytes transfected with Ad-SVV or Ad-GFP using propidium iodide staining for flow cytometry. As showed in Figure 2, 48 hours after overexpression of survivin there was a significant increase of the ratio of G2/M phase of the cell cycle, indicating that survivin may trigger cell cycle progression of cardiomyocytes.

Figure 2. Adenoviral overexpression of survivin in cardiomyocytes induces cell cycle progression. Neonatal cardiomyocytes were plated for 2 days then transfected with an adenovirus containing GFP or survivin for 48 hours. Cell cycle distribution was profiled and quantified using flow cytometry (c). *P<0.02
Cardiac pathology of a 30-month-old αMHC-survivin−/− mouse and a wild-type littermate control is presented. Echocardiography shows long-axis view with a large thrombus (*) in the right atrium and tricuspid regurgitation with an enlarged pulmonary trunk (black arrow, right ventricular inflow; black arrowhead, LV inflow). Note the massive enlargement and dilation of both ventricles and atria with fresh and old organized thrombi.

Figure 4. Cardiac specific survivin knockout causes early mortality and impairment of cardiac function. A, Survival analysis of 30 α-MHC-survivin−/− and 35 wild-type mice. B, Ejection fraction of wild-type and α-MHC-survivin−/− mice at 18 and 36 weeks was measured by cardiac MRI.

Next we showed that cardiac specific deletion of survivin caused early postnatal death of transgenic mice
due to a decreased amount of cardiomyocytes. We generated Cre-Lox-mediated α-myosin heavy chain (MHC)-driven cardiac specific survivin knockout mice and have found several interesting pictures in these mice—(1) there might be large thrombi in the right atrium and these mice showed enlarged atria and ventricles (Figure 3), (2) these survivin knockout mice had a lower survival rate after birth compared with wild-type littermates as examined at 10 weeks old (Figure 4) and the mean cardiac ejection fraction was decreased in survivin−/− mice at 18 and 36 weeks (Figure 4), and (3) the number of cardiomyocytes was lower in α-MHC-survivin−/− mice than in wild type mice, possibly due to a lower mitotic rate but not due to an increase of cardiomyocyte apoptosis (Figure 5). We also found the expression of survivin in falling human hearts supported by ventricular assist device (LVAD). These results imply survivin expression is required for cardiac development and maturation. Identifying signaling molecules regulating survivin expression in cardiomyocytes, both upstream and downstream, may thus lead to novel discovery of therapeutic targets for cardiac cell therapy.

Figure 5. Cardiomyocyte number is decreased in α-MHC-survivin−/− mice. A, Total cardiomyocyte numbers per heart. B, Quantification of mitotic figures in cardiomyocytes in newborn control and survivin-deficient hearts. Right, Cardiomyocyte mitosis in an α-MHC-survivin−/− mouse and a wild-type control. Data are expressed as box plots. °Outliers; *significant difference vs. wild type; #significant difference vs. 1-day-old α-MHC-survivin−/−.