

## Effect of flow velocity on Doppler signal of a single microbubble in laminar flow

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### 1. Introduction

Contrast enhanced active Doppler ultrasonography (CEADUS), where acoustic radiation force (ARF) enhances the translation of ultrasound contrast agents (UCAs), has been proposed for visualizing lymphatic vessels with intermittent slow flow. A spatiotemporal filter based on singular value decomposition (SVD) is expected to be decisive for imaging lymph vessels. The component selection based on the magnitude of singular value (singular-value-based algorithm) was typically conducted for discriminating clutter from dynamic components such as blood flow, where the threshold was often empirically determined. The discrimination based on the singular value is not likely effective if clutter signals and electrical noise with an intensity approximately the same as contrast echo are present, thereby determining based on the features of a frequency spectrum of a temporal singular vector (frequency-based algorithm) would be preferable. In this report based on phantom experiments, we investigate how the spectrum of the Doppler signal depends on the sparsely-flowing UCAs, and discuss what spectrum feature we should focus on to discriminate contrast echo from the others.

### 2. Materials and Methods

Sonazoid<sup>®</sup> was used as UCA. The contrast agent suspension was diluted so that the number per resolution volume was less than 1. A 0.91 mm diameter channel was formed in the gel containing the acoustic scatterer at an inclination angle of 15 deg, and ultrasound was transmitted and received in the presence of a downward flow. The flow rate was controlled by a syringe pump at 0.1 and 1 mL/min. Assuming a Hagen-Poiseuille flow, the flow velocity at the center of the channel was estimated to be about 5.1 and 51 mm/s.

**Figure 1** shows the sequence of ultrasound transmission, where conventional pulse inversion Doppler (PID) and burst-wave-aided CEADUS were executed in series. The former sequence had less effect of ARF, and the later enhanced the translation of UCAs in the direction of sound propagation due to the ARF caused by burst wave. The pulse repetition interval (PRI) and pulse burst interval

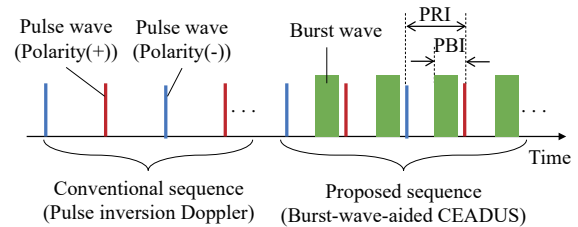


Fig. 1 Ultrasound transmission sequence

(PBI) were set to 0.1 ms and 0.05 ms, respectively. The center frequencies of the pulse and burst waves were 5.2 MHz and 7.5 MHz, respectively, and the length of burst wave was 350 cycles (approximately 47  $\mu$ s). The peak negative pressure of the pulse was 0.23 MPa. The total number of transmissions for each method was 202, and the time required for all transmissions was about 40 ms.

A programmable platform for developing ultrasound equipment (Vantage 256, Verasonics) and a 128-element linear array probe (L11-5v, Verasonics) were used for ultrasound transmission and reception. The frequency range of the probe was 4.68-10.52 MHz. Plane waves were transmitted using the sequence shown in Fig. 1, and the RF data was reconstructed by applying the delay-and-sum beamforming with the dynamic aperture. A spatiotemporal filter based on SVD was applied to the beamformed RF data (spatial 272, 200 pixels  $\times$  202 frames) to emphasize contrast echo. The components with -46 - -30 dB of singular-value magnitude, where 0 dB depicted the maximum of singular value, were tentatively selected for discriminating UCAs. Non-filtered Doppler signals of identified UCAs, i.e., the change of contrast echo in the frame direction, were analyzed in the frequency domain.

### 3. Results and Discussions

**Figure 2** shows images filtered by singular-value-based algorithm, the Doppler signals, and its normalized power spectrum (Doppler spectrum) of an identified UCA. Burst-wave-aided CEADUS shifted the peak of the Doppler spectrum to a negative frequency since UCAs moved away from the probe due to the acoustic radiation force. It was found that the Doppler spectrum at 0.1 mL/min had sharper peaks compared with those at 1 mL/min. This is because the duration UCAs pass through the

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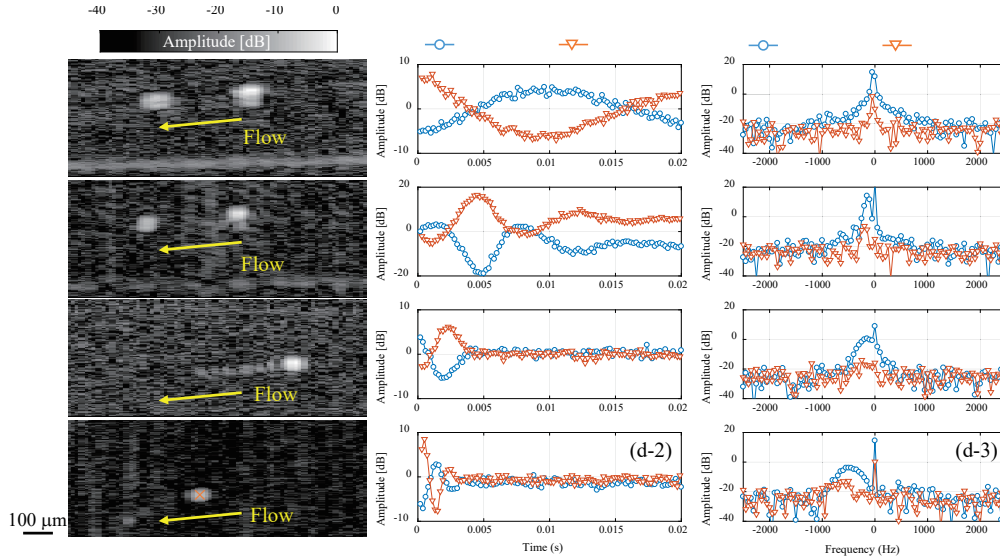


Fig. 2 (1) Clutter-filtered images by the singular-value-based algorithm and (2) Doppler signals for polarity(+) and polarity(-) at the symbol ‘x’ in (1), and (3) normalized power spectra of the Doppler signal for (a) PID sequence at 0.1 mL/min, (b) burst-wave-aided CEADUS sequence at 0.1 mL/min, (c) PID sequence at 1-mL/min, and (d) burst-wave-aided CEADUS sequence at 1 mL/min.

resolution volume shortened as the flow in the lateral direction became fast. As a result, the short length of the Doppler signal resulted in the broad peak of the spectrum.

This result suggested that the expected value ( $f_E$ ) and standard deviation ( $f_{SD}$ ) of normalized power spectrum of the Doppler signal would be features for discriminating flowing UCAs from clutter. Thus, we selected the components based on  $f_E$  ( $v_E$ ) and  $f_{SD}$  ( $v_{SD}$ ) of the frequency spectra of temporal singular vector, where  $v_E$  and  $v_{SD}$  denoted the velocities calculated by  $v = 2cf/(f_0+f)$ .  $c$  was the speed of sound, and  $f_0$  was the center frequency of transmitted ultrasound. **Figure 3** show the images filtered by the frequency-based algorithm. For PID sequence, the components with  $5 \text{ cm/s} < v_{SD} < 40 \text{ cm/s}$  was selected, and  $v_E$  was excluded assuming that the translational direction of UCAs was unknown. For burst-wave-aided CEADUS sequence,  $v_E$  was also a beneficial parameter for determining the components because UCAs always moved away from the probe, arising the negative frequency shift of Doppler spectrum. Thus, we chosen the components with  $-15 \text{ cm/s} < v_E < -0.5 \text{ cm/s}$  and  $1.5 \text{ cm/s} < v_{SD} < 40 \text{ cm/s}$ . Comparison between images in Figs. 2 and 3 demonstrated that frequency-based algorithm could achieve the contrast ratio same as the singular-value-based algorithm.

#### 4. Summary

Sparsely-flowing UCAs were visualized by a spatiotemporal filter based on SVD, where the frequency spectrum features of the temporal singular vector aided to select the contrast components. The

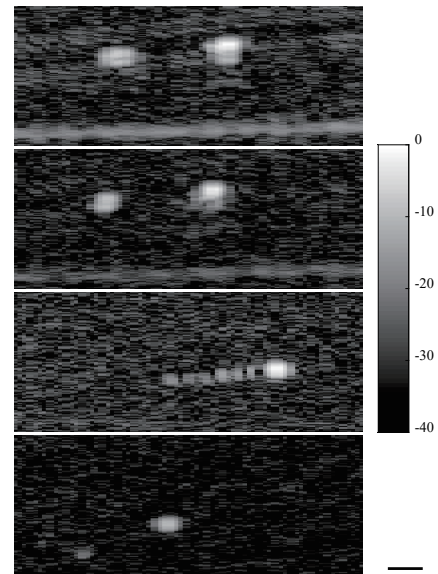


Fig. 3 Clutter-filtered images by the frequency-based algorithm for (a) PID sequence at 0.1 mL/min, (b) burst-wave-aided CEADUS sequence at 0.1 mL/min, (c) PID sequence at 1-mL/min, and (d) burst-wave-aided CEADUS sequence at 1 mL/min.

frequency-based algorithm gave the same clutter removal as the singular-value-based algorithm. In the future, we will investigate whether the frequency-based algorithm is effective when the tissue with the echo intensity approximately the same as UCAs are present around UCAs.

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