

2:00

**1pBA2. Uncoupling a bi-disperse microbubble population for decreased ULM acquisition times: A proof-of-concept study.** Giulia Tuccio (DISI, Univ. of Trento, via Sommarive, 5, Povo, Trento 38123, Italy, giulia.tuccio@unitn.it), Lisa te Winkle, Wim van Hoeve (Solstice, Enschede, Netherlands), and Libertario Demi (Information Eng. and Comput. Sci., Univ. of Trento, Trento, Italia, Italy)

Ultrasound Localization Microscopy (ULM) enables to accurately characterize micro-vascular structures by means of ultrasound imaging. In ULM, the backscattering signals of injected microbubbles (MBs) are utilized to sub-wavelength localize and track MBs flowing in the circulatory system. To ensure precise MB localizations, ULM is constrained to low MB concentrations, leading to prolonged acquisition times. Owing to patient comfort,

motion, and computational cost to elaborate data, the constraint on low MB concentrations is a bottleneck for ULM clinical translation. To mitigate the need of low MB concentration, we propose to uncouple a bi-disperse MB population. The bi-disperse population is composed of two monodisperse MB populations having diameter (and resonance frequency) of  $2.5\ \mu\text{m}$  (3 MHz) and  $3.8\ \mu\text{m}$  (5.5 MHz), respectively. The different diameter determines a different resonance response. Experiments are performed injecting the populations singularly and simultaneously in a 3-D printed phantom. Uncoupling is performed by means of a signal processing pipeline, which exploits the strong nonlinear response of MBs having resonance frequency tuned with the transmission frequency. After uncoupling, super-resolved density and velocity flow maps are generated for each MB population. The results demonstrate the capability of uncoupling the selected pair of MB populations, thus potentially permitting increased MB concentrations.

## Invited Paper

2:20

**1pBA3. Power Doppler and color flow imaging with null subtraction imaging.** Michael L. Oelze (Elec. and Comput. Eng., Univ. of Illinois Urbana-Champaign, 405 N Mathews, Urbana, IL 61801, oelze@illinois.edu) and Zhengchang Kou (Elec. and Comput. Eng., Univ. of Illinois Urbana-Champaign, Urbana, IL)

Null subtraction imaging (NSI) is a nonlinear beamforming technique that uses nulls in a beam pattern instead of the mainlobe to beat the diffraction limit. In this study, we used a 256-element linear array with  $55\text{-}\mu\text{m}$  pitch to image the microvasculature of a mouse brain using NSI and delay and sum (DAS) with plane wave compounding. We also explored combining pulse inversion (PI) with NSI, i.e., we transmitted pulses at center frequency of 15.6 MHz to obtain the second harmonic at 31.2 MHz. Color flow imaging (CFI) at the fundamental frequency was also generated using traditional methods and NSI and compared. Higher spatial resolution and contrast in power Doppler images were observed in the NSI images compared to DAS (spatial resolution of  $1/4\text{--}1/6$  of a wavelength). The CFI images constructed using NSI resolved small vessels with flows in opposite directions that were not observed in the CFI using DAS, where vessels of opposite flows appeared averaged together as one vessel due to lower spatial resolution. The computation time was increased by only 40% for NSI compared to DAS. No contrast agents were used in these images.

## Contributed Papers

2:40

**1pBA4. Gas vesicle expression in stem cells and the potential as a bio-marker application.** John Kim (Mech. Eng., Univ. of Michigan, 3033 LENOX RD NE, # 23311, Atlanta, GA 30324, kjohnw@umich.edu), Alessandro R. Howells (Biomedical Eng., The Penn State Univ., State College, PA), Xiaojun Lian (Biomedical Eng., The Penn State Univ., University Park, PA), and Chengzhi Shi (Univ. of Michigan, Ann Arbor, MI)

Gas vesicles (GVs) are highly promising contrast agents that have been actively investigated throughout the development of contrast agents. Unlike chemically synthesized materials, GVVs offer distinct advantages in bio-related studies due to their biocompatibility, making them a safer alternative to existing agents. GVVs are gas-filled structures found in microorganisms, enabling their host to remain buoyant in aqueous environments. Since GVVs are composed of gas vesicle proteins, it is possible to genetically encode specific cell lines to express gas vesicles at will. However, whether these cells can be utilized in clinical trials to self-contain contrast agents has not been fully explored. In recent years, we have been investigating efficient methods to express GVVs in stem cells, which could function as a repeatable contrast agent. To achieve this, we employed a drug selection technique to isolate stem cells that contain gas vesicle genes. Traditional isolation methods required fluorescence-activated cell sorting (FACS) followed by single-cell cloning, which was time-consuming and costly. These findings may guide researchers in cultivating GV-containing stem cells, potentially differentiating them into desired cell types for implantation into organs that require biomarkers.

3:00–3:20 Break

3:20

**1pBA5. Generation of modulators for super-resolution imaging.** Jian-yu Lu (Bioengineering, The Univ. of Toledo, 2801 West Bancroft St., Toledo, OH 43606, jian-yu.lu@ieee.org)

Medical ultrasound imaging has a trade-off between the lateral image resolution and penetration depth. Using the Point Spread Function (PSF) modulation super-resolution imaging method developed recently (Lu, IEEE TUFFC 2024), it is possible to overcome such a limit. To implement the method, an ultrasound array transducer such as a one-dimensional (1-D), two-dimensional (2-D), or annular array transducer can be used to produce a shear wave deep in the biological soft tissues. The shear wave is then focused to form a modulator of a size of about one half of the shear wave wavelength. Notice that since the speed of sound of the shear wave is much smaller than that of the longitudinal waves, the shear wave wavelength can be small. Finally, the modulator is used to induce a phase modulation to the imaging wave for super-resolution ultrasound imaging. In this work, the mechanism of shear wave focusing is studied both theoretically and through computer simulations. The results show that it is possible to focus a shear wave to achieve a wave feature of about a half wavelength of the shear wave, opening up a possibility for super-resolution ultrasound imaging deep in the biological soft tissues.