Modeling the Non-Linear Microbubble Response to Coded, Multi-Pulse Sequences

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Introduction:

- Microbubbles (fig. 1) are used in Ultrasound (US) imaging as contrast agents to better visualise blood flow. They consist of an inert gas encapsulated within a polymer, albumin or lipid shell and are 3-5 µm in diameter.
- After intravenous injection the microbubbles traverse the vascular system and can improve the diagnostic utility of US by allowing perfusion imaging and quantification of blood flow, enabling improved sensitivity and specificity in tumor diagnosis (fig. 2) [1].

- Due to the fragile nature of microbubbles, either a signal shot destructive imaging mode (fig 2.) [1] or a low power (lower sensitivity) approach must be used. The aim of this work is to improve the sensitivity of US microbubble imaging while maintaining low acoustic powers.
- Pulse encoding techniques used in ultrasound imaging preserve axial resolution whilst allowing an increased energy input resulting in a significant increase in the signal-to-noise ratio (SNR) [2].
- Multi-pulse sequences that combine pulse inversion and amplitude modulation (PIAM) have been shown to yield high sensitivity to the non-linear scattering by microbubble contrast agents [3].
- We have shown experimentally that combining frequency modulated pulses (chirps) with PIAM sequences can further improve the sensitivity of ultrasound to microbubbles though we hypothesize that its non-linear response is associated with a degradation in the axial resolution.

Methods:

- A modified Rayleigh-Plesset [4] model was used to simulate the non-linear response of microbubbles to Chirp PIAM sequences.
- High speed optical images of oscillating microbubbles were recorded and used to parameterize the bubble model for SonoVue® (fig 3.).
- The effect of the non-linear microbubble response on the compression and cancellation post processing stages were investigated.
- Comparisons were made to corresponding short pulse PIAM sequences.
- Tradeoffs between SNR and axial resolution for different Chirp PIAM time-bandwidth products were examined.
- Sidelobes generated in the compression process (which are responsible for image artefacts) were studied to develop methods for its minimisation.

Results:

- Chirps tuned to the bubble resonant frequency (Fig. 4b) minimise the sidelobe and result in a stronger signal after processing.
- Narrowing the chirp bandwidth to match the microbubbles frequency response (Fig. 4c) allows an increase in SNR and further reduces the sidelobe level (Fig. 4d) as less chirp frequencies overlap the bubbles subharmonic frequency.
- Over short pulse PIAM, Chirp PIAM improves SNR (Fig. 5a), with best improvement at the highest pressures. The resolution of the Chirp PIAM sequence is always worse than PIAM though it does improve with increasing insonation pressure (Fig. 5b).

Conclusion:

- In agreement with our experimental observations, the detection of microbubbles can be enhanced using Chirp PIAM sequences over short pulse PIAM sequences as it preserves the extra energy it has after scattering and post processing.
- Chirp parameters can be manipulated to further increase SNR though there is a tradeoff for resolution.
- Sidelobe artefacts formed in post processing can also be minimised.

References:


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