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Acoustic unsteadiness of sprays from pressurised metered-dose inhalers

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Abstract

A technique has been developed for the measurement of acoustic unsteadiness of sprays from pressurised metered-dose inhalers. An ensemble ($n \geq 126$) of acoustic measurements of sprays were obtained for two formulations with and without ethanol. Acoustic signals were analysed using the Hilbert-Huang Transform to obtain their amplitude envelopes, allowing the instantaneous energy to be determined. Ensemble statistics of each formulation's instantaneous energies allowed the determination of time-variant unsteadiness. The performance of the technique is demonstrated using two formulations with different steadiness characteristics; internal flow pattern phase contrast visualisations are presented that show the flow pattern varies by formulation. Unsteadinesses are presented for both formulations and is approximately 50% higher for the propellant-only formulation in the first 100 ms of injection. Variation of the unsteadiness with low-pass filtering of the acoustic energy demonstrates that the unsteadinesses are more separable when short-duration fluctuations are removed.

Introduction

Unsteadiness affects the performance of twin-fluid atomisers (Jedelsky and Jicha 2008). The unsteadiness is closely related to the flow pattern at the nozzle exit orifice. Flows that exhibit temporal inhomogeneity of the flow in the nozzle exit orifice tend to be unsteady. Pressurised metered-dose inhalers (pMDI) are flash atomisers in which a drug-containing formulation is discharged from a nozzle. The discharge from the nozzle is predominantly vapour (Mason-Smith et al. 2016) and the liquid phase is often multicomponent, as cosolvents are added to the propellant.

Measuring unsteadiness has been accomplished in several ways. Frameworks exist that directly measure the unsteadiness (Edwards and Marx 1995). The framework developed by Jedelsky and Jicha (2008) uses pressure fluctuation measurements in the mixing chamber to estimate the fluctuation of the gas-liquid ratio at the nozzle; this is termed the 'two-phase flow unsteadiness'. Recent work (Sun et al. 2016) has shown that fluctuations of acoustic energy, which can be described as the 'acoustic unsteadiness', provide an indication of the flow unsteadiness. In this paper we extend the acoustic unsteadiness method of Sun et al. (2016) for use as a diagnostic for pMDIs. Two formulations are studied that exhibit highly different internal flow patterns, and their acoustic unsteadinesses are measured using the method outlined in this paper.

Methodology

A linear solenoid-driven rig was used to remotely actuate pMDI canisters. Phase contrast imaging was performed at the 7-ID beamline of the Advanced Photon Source at Argonne National Laboratory. Details of phase contrast imaging for fluid mechanics studied are given in Kastengren and Powell (2014).

Formulation	p_v (bar)	ρ_l $(\mathrm{kg/m^3})$
HFA134a	6.65	1208
HFA134a/Ethanol	5.95	1119

Table 1: Vapour pressures p_v and saturated liquid densities ρ_l of formulations studied.

Acoustic measurements were obtained in the Laboratory for Turbulence Research and Combustion (LTRAC). Lab temperature was monitored and was 22.4–23.9°C. A GRAS 46BE preamplified freefield microphone was connected to a National Instruments 16-bit analog-to-digital converter and was sampled at 250 kS/s. No antialiasing filter was used. The microphone was placed 23 mm from the nozzle exit orifice in the horizontal plane at an angle of 135° to the spray axis.

Two formulations were used and are tabulated in Table 1. Vapour pressures were estimated using the data provided in Gavtash et al. (2015). These two formulations had comparable vapour pressures and densities, but exhibited very different internal flow patterns. Phase contrast images of the internal flow structure in the expansion chamber and nozzle of the pMDI are shown in Figure 1. The propellant-only formulation contains large nonspherical bubbles with characteristic lengths almost equal to the expansion chamber diameter. In the parlance of multiphase flow patterns, this can be designated a slug/annular flow (Brennen 2005). By contrast, the ethanol-containing formulation is a bubbly flow with much smaller spherical bubbles on the order of 250 µm. Unsteadiness is highest for slug-type flows, as exhibited by the propellant-only formulation; bubbly flows with small bubbles relative to the size of the nozzle are most stable. Optical extinction measurements of these same formulations found a lower coefficient of variation for the ethanol-containing formulation, indicating a steadier spray process (Mason-Smith et al. 2015a). Similarly, the coefficient of variation of the optical extinction of HFA227ea sprays from a pMDI analogue were substantially reduced by the inclusion of ethanol (Mason-Smith et al. 2015b). The formulations listed in Table 1 are used as test cases for the acoustic unsteadiness technique.

Acoustic Analysis

Acoustic unsteadiness is the coefficient of variation (σ/μ) of the acoustic energy E (Sun et al. 2016). For continuous sprays, the mean and standard deviation of the acoustic energy can be obtained from a single spray record. As the pMDI spray is transient, we obtain these statistics from an ensemble of spray records and define the time-variant unsteadiness $U(t)$:

$$U(t) = \frac{\left\langle E^2(t) - \langle E(t) \rangle^2 \right\rangle^{1/2}}{\langle E(t) \rangle} \tag{1}$$

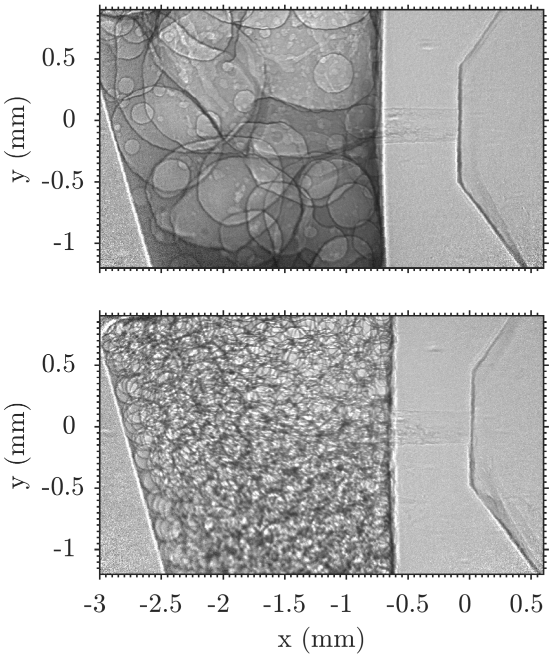

Figure 1: Phase contrast images for sump and nozzle flow 50 ms after start of injection of (top) HFA134a and (bottom) HFA134a/Ethanol.

The energy of the signal at time t is obtained by squaring the signal's instantaneous amplitude $a(t)$:

$$E(t) = a^2(t) \tag{2}$$

Defining the time-variant amplitude $a(t)$ of a non-stationary signal requires a non-stationary analysis technique. The Hilbert Huang transform (HHT) is a well-established method for analysis of non-stationary and nonlinear time series (Huang et al. 1998). A brief overview of the method is given.

The signal is decomposed into intrinsic mode functions (IMF) using the empirical mode decomposition (EMD) outlined in Huang et al. (1998). An analytic representation of each IMF is obtained by taking its Hilbert transform:

$$Y_i(t) = \frac{1}{\pi} P \int_{-\infty}^{\infty} \frac{X_i(t')}{t - t'} \mathrm{d}t' \tag{3}$$

where X_i is the i_{th} IMF and P is the Cauchy principal value. The instantaneous amplitude a of the IMF is obtained trigonometrically:

$$a_i(t) = \left[X_i^2(t) + Y_i^2(t)\right]^{1/2} \tag{4}$$

The instantaneous amplitude of the signal is then obtained by summing the amplitudes of the modes:

$$a(t) = \sum_{i=1}^{N} a_i(t) \tag{5}$$

With an ensemble of instantaneous amplitudes, the unsteadiness can be evaluated.

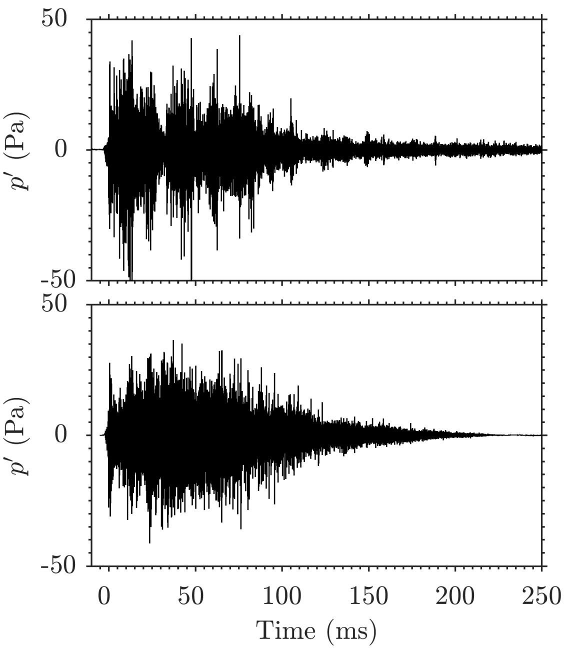

Figure 2: Acoustic signals from sprays of (top) HFA134a and (bottom) HFA134a/Ethanol.

Results and Discussion

Sample signals of the acoustic pressure fluctuation p' for each formulation are shown in Figure 2. Injections are approximately 100-200 ms in duration. For the propellant-only formulation, sound of relatively constant low amplitude is generated from 125-250 ms, and is related to the discharge of vapourous propellant from the expansion chamber. The ethanol-containing formulation has a more rapid end-of-injection event, with a continual decline in the amplitude from 50 ms until it is no longer discernible at 225 ms. Both formulations show spikes in the acoustic amplitude, likely to be associated with the passage of bubbles from the nozzle exit orifice. The propellant-only signal shows a local minimum around 30 ms. Collection of an ensemble of spray records enables the determination of which of these variations in amplitude are stochastic and which are repeatable.

Determination of the unsteadiness requires an accurate estimation of the variance of the acoustic energy, and may provide erroneous estimates in the presence of noise. The presented measurements have very high signal-to-noise ratios, demonstrated by the absence of discernable pressure fluctuations before the start of injection. The RMS amplitude of the noise is approximately 0.15 Pa, which corresponds to a peak signal-to-noise ratio of 10^5.

Signals were decomposed into IMFs with the EMD and their amplitude envelopes reconstructed with the first two IMFs. This reconstruction acted as a high-pass filter with a cutoff of approximately 20 kHz; as the frequency in each mode varies as a function of time, some energy associated with frequencies above the cutoff may be contained in the third mode. An example of the agreement between the amplitude envelope and the raw signal is shown in Figure 3.

Statistics of the acoustic energy were calculated for each formulation at full temporal resolution. The resulting mean, RMS and unsteadiness are binned to 1 ms increments and are shown in Figure 4. The mean acoustic energy plot shows that the local minimum at 30 ms of the pressure fluctuation for the propellant-only formulation (Figure 2, top) is repeatable across the ensem-

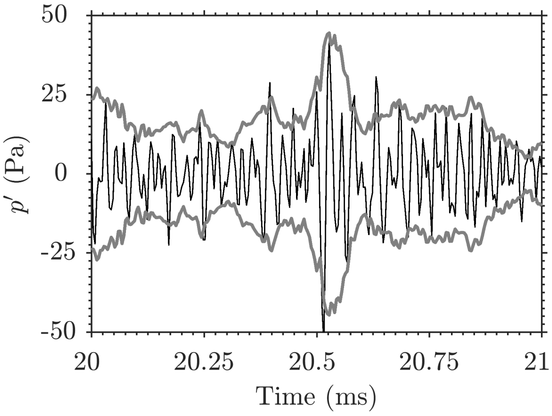

Figure 3: Short time segment of HFA134a spray acoustic signal and signal envelope $\pm a(t)$ (shown in gray).

ble. A local minimum of the droplet velocity for pure propellant pMDI sprays occurs around this same time (Myatt et al. 2015), and phase contrast videos show that this corresponds to the time required to evacuate air from the expansion chamber. Importantly, this demonstrates that the time-variant unsteadiness method separates repeatable and random fluctuations of the acoustic amplitude, which would be aggregated in a quasi-steady state implementation of the Sun et al. (2016) method. For the ethanol-containing formulation, mean acoustic energy rises until a maximum at approximately 30-35 ms and exhibits a gradual decay. The propellant-only formulation amplitude decays after a local maximum at approximately 50 ms.

RMS acoustic energy and unsteadiness are presented in Figure 4 (middle and bottom, respectively). The RMS acoustic energy traces are similar in shape to the mean acoustic energy. This results in a near-constant value of the acoustic unsteadiness. For both formulations the unsteadiness values are high, the propellant-only spray having an unsteadiness of around 1.2 during the first 100 ms of the injection. The ethanol-containing formulation has a lower unsteadiness, remaining almost invariant at 0.8 throughout this same time period.

Short-time variability of the acoustic energy prompted Sun et al. (2016) to low-pass filter the unsteadiness measurement by integrating the acoustic energy over a time T^*, noting that its selection was important to the measurement. For their study, the integration time was chosen to be 30 ms, with little explanation given for its selection. One interpretation is that time integration acts as a low-pass filter on the acoustic energy and enables separation of flow regimes above a selected time scale. Bubbly flows are unsteady on very short time scales associated with the passage of individual bubbles, and the accompanying fluctuation of the gas-liquid ratio at the nozzle exit orifice. These same flows will however be steadier at longer timescales—as will all flows, given the known effect of low-pass filtering on variance (Bendat and Piersol 1986). For a continuous spray process, the time scales of the unsteadiness could be obtained with spectra of the mean-subtracted acoustic amplitude. For transient spray processes, obtaining a time scale of the unsteadiness is not so straightforward. Investigating the effect of low-pass filtering the unsteadiness is one approach to indicate time scales associated with the fluctuations. To this end, we investigate the sensitivity of U to low-pass filtering.

The sensitivity of the unsteadiness measurement to low-pass filtering of the acoustic energy by binning is illustrated in Figure 5. The plot shows the ensemble unsteadiness time-averaged over the interval 25-75 ms as a function of bin width, to a max-

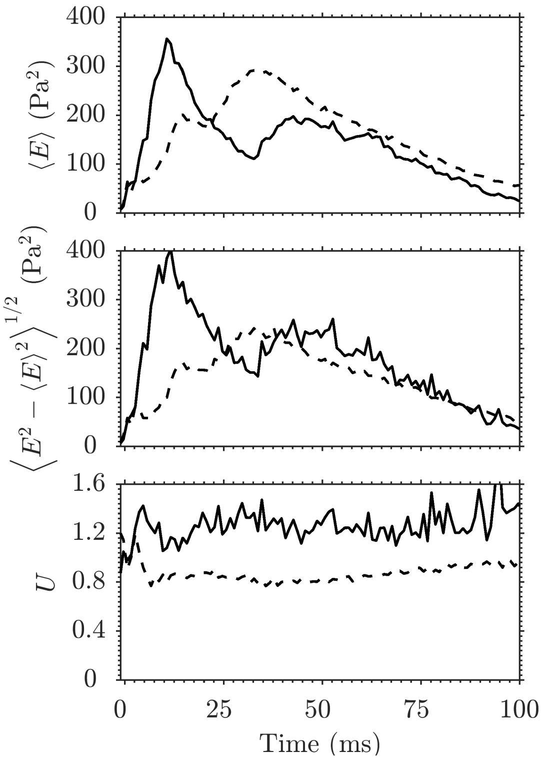

Figure 4: Ensemble (top) mean, (middle) RMS and (bottom) unsteadiness of E with (solid line) HFA134a and (dashed line) HFA134a/Ethanol formulations.

imum width of 2 ms. $\bar{U}$ is seen to be almost invariant at small bin widths below approximately 30 µs. Logarithmic axes are used to show that the RMS energy and the unsteadiness decay at a constant amplitude ratio (dB) per octave above 30 µs bin widths. Over this range, the unsteadiness decays with an amplitude ratio of 1.18 per octave for the propellant-only case and 1.3 for the ethanol-containing formulation. At larger bin widths, the formulations become more separable as the ratio of their unsteadinesses increases. The difference in decay rates of unsteadinesses suggests that more energy is concentrated on shorter timescales for the ethanol-containing formulation, consistent with the bubbly flow regime depicted in Figure 1. If the random fluctuations for the ethanol-containing case are associated with the passage of individual bubbles, low-pass filtering these fluctuations will provide an unsteadiness indicative of longer-period fluctuations—such as those from the passage of large liquid slugs in the propellant-only formulation.

Conclusions

A method is developed for the measurement of acoustic unsteadiness of sprays from pressurised metered-dose inhalers. The method is able to separate random and repeatable fluctuations of the amplitude of the signal. Unsteadiness is near-constant for each formulation during the first 100 ms of injection and was approximately 50% higher for the propellant-only formulation. The measured unsteadiness is sensitive to low-pass filtering of the acoustic energy, and decays more rapidly with filter width for the bubbly flow case than for the slug-annular flow case.

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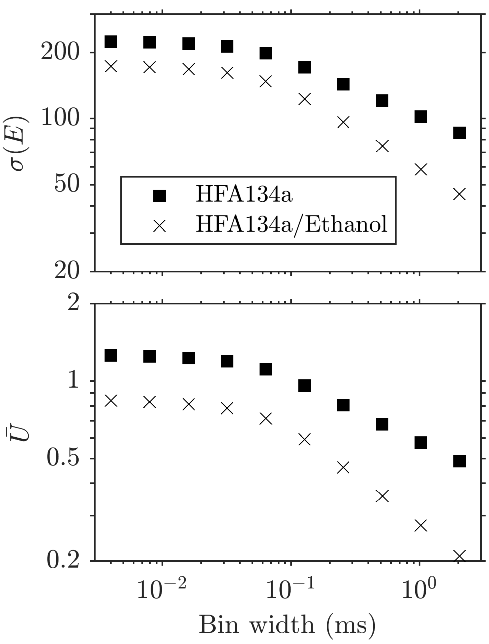

Figure 5: Effect of filter width on U averaged over the interval 25-75 ms.

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