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Ultrasound-Driven Megahertz Faraday Waves for Generation of Monodisperse Micro Droplets and Applications

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Abstract

Our theoretical findings on instability of Faraday waves at megahertz (MHz) drive frequency and realization of silicon-based MHz multiple-Fourier horn ultrasonic nozzles (MFHUNs) together have enabled generation of mono-disperse droplets of controllable diameter (2.5-6.0 μm) at very low electrical drive power (<0.5 Watt). The resulting battery-run clogging-free droplet generator has imminent application to pulmonary (inhalation) drug delivery and other potential applications. Here an update of advances on analysis and design of the MHz MFHUNs and the underlying physical mechanism for generation of mono-disperse micro droplets, and the nebulizer platform for application to detoxification of cyanide poisoning are presented.

Keywords: Faraday instability, multiple-Fourier horns, monodisperse micro droplet, pulmonary drug delivery, cyanide poisoning

1. Introduction

A number of ultrasonic techniques for generation of micro droplets, for examples, the micro-machined droplet generators based on a liquid horn structure (Meacham et al., 2004) and piezo-electrically actuated flex-tensional micro-machined transducers (Perçin et al., 2002; Kwon et al, 2006) were reported. Current commercial ultrasonic nebulizers produce droplets of uncontrollable and very broad size distributions (polydisperse). Here we present a new technique for generation of controllable monodisperse droplets of desirable diameter range (2.5 to 6.0 μm) using Faraday waves excited by ultrasound with MHz multiple-Fourier horns (MFHs) in cascade and in resonance.
Faraday waves were first observed as wavy surface of a water layer resting on an elastic planar solid support subjected to perpendicular vibration, as depicted in Fig. 1a, at a very low drive frequency of 5 Hz (Faraday, 1831), and analyzed (Rayleigh, 1883). Faraday instability, the underlying physical mechanism for Faraday wave formation and amplification, was studied extensively based on Faraday’s planar geometry, but mostly at very low drive frequencies ranging from tens to thousands hertz (Hz). See the references cited in (Cerda and Tirapegui, 1997; Tsai and Tsai, 2013). At such low drive frequencies, various standing-wave patterns were observed when the vibration amplitude (displacement) on the solid surface reached the onset threshold for Faraday wave formation. However, in the few reports on experiments at such low drive frequencies droplet ejection was found to take place only when the vibration amplitude on the solid surface was much higher than the onset threshold for Faraday wave formation (Yule, 2000). In stark contrast, our recent discovery as presented here shows that at the much higher drive frequencies of MHz the onset threshold for Faraday wave formation is much lower and the vibration amplitude required for subsequent droplet ejection is only slightly higher than the onset threshold for Faraday wave formation.

2. Theory and technique

2.1. Excitation of Enhanced Ultrasonic Vibration at MHz using Multiple-Fourier Horns in Resonance

Silicon-based multiple Fourier horns (MFHs) in cascade and vibrating at a single resonance frequency at MHz (Fig. 1b) is used to facilitate Faraday’s classical low-frequency experiment at MHz drive frequency. The resulting multiple-Fourier horn ultrasonic nozzle (MFHUN) with its Z-axis along the <110> direction of the silicon wafer is fabricated using the MEMS technology (Tsai et al., 2009). The nozzle consists of a drive section and a resonator section. A lead zirconate titanate (PZT) piezoelectric transducer is bonded on the drive section to excite mechanical vibrations along the nozzle axis (Z-axis). The resonator section is made of MFHs in cascade. Each horn is of half wavelength design. The nozzle is designed to vibrate at a single resonance frequency of the MFHs. The resultant vibration amplitude (displacement) on the nozzle end face (tip of the distal horn) is greatly enhanced with a gain of $M^a$ for a n-Fourier horn nozzle in which $M$ is the magnification of displacement for each horn (Tsai et al., 2009).

A 3-D finite element method simulation is carried out first for vibration mode shape analysis and then for electrical impedance analysis. The former determines the nozzle resonance frequency of pure longitudinal vibration mode; the latter determines the longitudinal vibration amplitude on the nozzle end face and the electrical impedance at the resonance frequency (Tsai et al., 2009). The simulated vibration amplitude (at electrode voltage of 1.0 V) is then used to determine the threshold voltage required to produce the onset threshold of vibration amplitude ($h_{cr}$) for Faraday wave formation and droplet ejection. Finally, the threshold voltage thus obtained together with the resistive part of the impedance determined is then used to calculate the electrical drive power required for droplet ejection.

2.2. Linear Theory on Temporal Instability of MHz Faraday Waves for Droplet Ejection

The enhanced longitudinal vibration amplitude on the end face of the MFHUN exerts a periodic pressure on the resting liquid layer depicted in Fig. 1(b). Faraday waves, under an external periodic acceleration $h(2\pi ft)^2\cos(2\pi ft)$, are formed on the free surface of the liquid layer when the peak vibration amplitude of the nozzle end face ($h$) reaches the onset threshold ($h_{cr}$). The theoretical treatment based on linearized Navier-Stokes equations for incompressible Newtonian liquids with density $\rho$, surface tension $\sigma$, and kinematic viscosity $\nu$ (Tsai and Tsai, 2013) results in temporal evolution of the Faraday wave amplitude $\xi_k$ of the $k^{th}$ mode:
\[ \xi_k(t) = \xi_0 e^{\pi k f (h - h_{cr})} \sin(2\pi(f/2)t - \pi/4), \]  

where the wave number \( k = 2\pi/\lambda \), the wave frequency \( \omega_k^2 = \sigma k^3 / \rho \), \( \xi_0 \) is the initial wave amplitude, and \( h_{cr} \) is:

\[ h_{cr} = 2\pi k / (\pi f) = 2\nu \rho^{1/3} (\pi \sigma)^{1/3} f^{-1/3}. \]

Eq. (2) shows the specific dependence of the onset threshold on the drive frequency \( f \) and the liquid properties \( \rho, \sigma, \) and \( \nu \). It is important to emphasize that \( h_{cr} \) decreases with the drive frequency in accordance with \( f^{-1/3} \), and the wave amplitude \( \xi_k(t) \) grows exponentially in time when \( h > h_{cr} \). While \( h_{cr} \) decreases with the drive frequency in accordance with \( f^{-1/3} \), the exponent \( \pi k f (h - h_{cr}) \) of Eq. (1) in a time increment of 0.4ms is \( \approx 2 \times 10^{11} \) times that with \( h - h_{cr} \) as large as 100\( \mu \)m at 200 Hz drive frequency and a low periodic acceleration of 16\( g \) (Yule and Al-Suleimani, 2000) at the same time increment (0.4ms). The amplitude growth rate factor at 2.0 MHz with \( h - h_{cr} \) of 0.01\( \mu \)m in a time increment of 0.4ms is still greater (by 8%) than that at 200 Hz with \( h - h_{cr} \) of 100\( \mu \)m in a much longer time increment of 185ms. Thus, the wave amplitude at 2 MHz drive frequency grows very rapidly and when it becomes too great to maintain stability the Faraday waves break up to result in ejection of droplets from the free surface of the liquid layer. Fig. 2 shows a stream of droplets issuing from the endface of a 4-Fourier horn 2 MHz nozzle at atomization frequency of 1.921 MHz, output rate of 200\( \mu \)L/min, and electrical drive power of 0.2 W. Note that the liquid (water) was transported to the nozzle endface through a silica tube and a 50\( \mu \)m liquid layer was maintained during atomization.

The theoretical droplet diameter \( (D_p) \) in terms of Faraday wavelength \( (\lambda) \) is as follows (Tsai and Tsai, 2013):

\[ D_p = 2(2 / \pi^2)^{1/3} (\sigma / \rho)^{1/3} f^{-2/3} = 0.40\lambda \]

Clearly, for a given liquid to be atomized, the desired size of the droplets can be controlled by the drive frequency \( f \) of the MFHUN in accordance with \( f^{-2/3} \); the higher the nozzle drive frequency the smaller the droplet size. The size and size distribution of the droplets (aerosols) produced by the 2.0 MHz nozzle (Fig. 2) was measured using Malvern/Spraytec size analyzer (Model #STP 5311). The measured droplet diameter is 3.4\( \pm \)0.3\( \mu \)m in good agreement with the predicted value of 3.2 \( \mu \)m which can be significantly smaller for low surface tension medicines.

In summary, all the experimental data including controllable micron-size droplet diameter, narrow size distribution, and very low electrical drive power are in excellent agreement with the predictions of the linear theory.
3. Applications to inhalation drug delivery

The droplet generator presented has demonstrated imminent application to inhalation drug delivery and other applications such as nanoparticle synthesis, processing for electronic and photonic nano-structures can be envisaged. Inhalation is an important route for non-invasive drug delivery. Drugs designed to treat pulmonary diseases or for systemic absorption through the lung require optimum particle size (2 to 6μm) to target delivery (Patton and Byron, 2000). Therefore, control of aerosol size plays a critical role in the efficient and effective delivery of medications. Even the advanced commercial devices using vibrating mesh technology still suffer from broad aerosol size (polydisperse) distributions and lack of size-control capability, and are also plagued by clogging of the orifices of the mesh used. The battery-run pocket-size nebulizer realized earlier using a single MFHUN was used successfully to aerosolize a variety of common pulmonary drugs (Tsai et al., 2014). Controllability of particle (aerosol) size range (2.5 to 6μm) and much narrower size distribution demonstrated by the new nebulizer will improve targeting of treatment within the respiratory tract and improve delivery efficiency. For example, a recent in-vitro experiment with Technetium (Tc) -tagged saline solution has demonstrated higher delivery efficiency than the existing commercial nebulizers (Diaz et al., 2012).

Short treatment time is a critical requirement in acute situations such as massive cyanide poisoning (Tsai et al., 2012). Clearly, the treatment time can be shortened by increased aerosol output rate of an array of MFHUNs. Furthermore, nozzle arrays with individual nozzles operating at identical or different drive frequency will provide the unique capability for simultaneous formation of aerosols of the same or different medicines at identical or different aerosol sizes. Such strategy is essential in order to avoid instability of mixed drug solutions prior to aerosolization. A battery-run pocket-size nebulizer with twin-nozzles as shown in Fig. 3 was constructed most recently to demonstrate simultaneous nebulization of cobinamide and magnesium thiosulfate antidotes for detoxification of cyanide poisoning. Specifically, for 115 mM cobinamide and 1 M magnesium thiosulfate antidote solutions, simultaneous and continuous aerosolization each at a flow rate of 250 μL/min for 5 min delivered 430 mg thiosulfate and 155 mg cobinamide that would be sufficient antidote dosages for effective detoxification of cyanide poisoning.

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References

Cerda, E.A., E. L. Tirapegui, 1997. Faraday’s instability for viscous liquids. Phys. Rev. Lett., 78, 859-862.
Diaz, K.T., S. Skaria, K. Harris, M. Solomita, S. Lau, K. Bauer, G.M. Smaldone, R. Condos, 2012. Delivery and safety of inhaled interferon-γ in idiopathic pulmonary fibrosis. J. Aerosol Medicine and Pulmonary Drug Delivery, 25, 79-87.
Faraday, M., 1831. On a peculiar class of acoustical figures and on certain forms assumed by groups of particles upon vibrating elastic surfaces. Phil. Trans. Roy. Society, London, A52, 299-340.
Kwon, J.W., H. Yu, Q. Zou, E.S. Kim, 2006. J. Micromech. Microeng. 16, 2697-2704.
Meacham, J.M., C. Ejimofor, S. Kumar, F.L. Degertekin, A.G. Fedorov, 2004. Rev. Scientific Instruments, 75, 1347-1352.
Patton, J.S., P. R. Byron, 2007. Inhaling medicines: delivering drugs to the body through the lungs. Nat. Rev. Drug Discovery, 6, 67-74.
Percin, G., B.T. Khuri-Yakub, 2002. IEEE Trans. on Ultrasonics/ Ferroelectrics and Frequency Control, 49, 573-584 and 585-595.
Rayleigh, B., 1883. On the crispation of fluid resting upon a vibrating support. Phil. Mag., 16, 50-58.
Tsai, S.C., C. H. Cheng, N. Wang, Y. L. Song, C. T. Lee, C. S. Tsai, 2009. Silicon-based Megahertz ultrasonic nozzles for production of monodisperse micrometer-sized droplets. IEEE Trans. Ultrason. Ferroelect. Freq. Control (UFFC), 56, 1968-1979.
Tsai, C.S., R.W. Mao, S.K. Lin, N. Wang, S.C. Tsai, 2010. Lab on a Chip, 10 2733-2740.
Tsai, S.C., S.K. Lin, R.W. Mao, C.S. Tsai, 2012. Phys. Rev. Lett., 108, 154501-154501 to -154505.
Tsai, S.C., R.W. Mao, Y. Zhu, E. Chien, J. Maduzia, C.S. Tsai, M.Brenner, S. Mahorn, D. Muka, G. Boss, and S. Patterson, 2012. Proc. of the IEEE Int. Ultrasonics Sym. (IUS-2012), 1632-1634.
Tsai, S.C., C.S. Tsai, 2013. Linear theory of temporal instability of megahertz Faraday waves for monodisperse microdroplet ejection. IEEE Trans. UFFC, 60, 1746-1754.
Tsai, C.S., R.W. Mao, S.K. Lin, Y. Zhu, S.C. Tsai, 2014. Faraday instability-based micro droplet ejection for inhalation drug delivery. TECHNOLOGY, 2, 75-81. http://www.worldscientific.com/worldscinet/technology.
Yule, A.J., Y. Al-Suleimani, 2000. Proc. of Royal Society of London A, 456, 1069-1085.