Detection of microbubble trajectories on M-mode images using Kalman filtering

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Abstract—Ultrasound Contrast Agents (UCA) are widely used for the diagnosis of cardiovascular diseases. They typically consist of shell encapsulated microbubbles which, when injected in blood, increase the blood/tissue ratio in ultrasound medical images. Characterizing the behavior of microbubbles hit by US energy, is important to optimize their performance in clinical applications. In this paper, the movement of microbubbles pushed away from US probes by the radiation force is considered. A simple experimental set-up is used to obtain Mmode images in which each microbubble describes a trace of variable brightness position and slope.

A Kalman filter model allows an iterative estimation of the instantaneous values of variables such as the bubble position, velocity and acceleration, in a discrete time process. The model constrains the solution of the estimation by two control parameters: the variance of acceleration and the maneuverability, characterizing the bubble inertia.

The accuracy of the method has been evaluated on artificial images reporting different phenomena: trace crossing, intensity variation, sudden interruption and different background noise levels. In most cases, the traces have been detected with a mean error lower than one pixel.

I. INTRODUCTION

Ultrasound contrast agents which consist of shell encapsulated microbubbles, are a great medical interest for both diagnostic and therapeutic purposes. In ultrasound equipment, the B-mode display is typically used, which provides a global visualization of a bubble population suspended in blood. Different approaches are necessary to investigate the reaction of individual microbubbles to US field. For example, high speed cameras capable of providing millions of frames per second can be used [1].

This paper presents a new method exploiting a simple experimental set-up based on a standard US transmitted / receiver device coupled to a computer [2]. The echo signals produced by microbubbles suspended in a water tank are visualized through a classic time motion (M-mode) display. Each microbubbles produces a trace whose time behavior depends on the microbubble physical characteristics as well as to the impinging acoustic field. Hence, tracking the microbubble trajectory in conditions of controlled acoustic excitation can be helpful for UCA characterization purposes. The first part of section II describes the experimental set-up used to obtain M-mode images from a suspension of microbubbles interrogated by a US burst. The image processing method developed for the tracking of the instantaneous position, velocity and acceleration of the bubbles is then reported. Finally, section III reports the results obtained by processing both simulated and experimental M-mode images.

II. METHOD

A. Experimental Setup

The experimental setup consists of a standard US pulsedwave (PW) system used to insonify still water in a tank. The liquid holds a low concentration $(10 \ \mu g/l)$ of thermoplastic microbubbles (Matsumoto Yushi-Seiyaku, Osaka, Japan) used to mimic the ultrasound contrast agents (UCA). Because of the US radiation force [3] the microbubbles are pushed away from the probe at an extent depending on the ultrasound pressure distribution along the beam axis and on the bubble properties.

For each transmitted burst (probe frequency: 4 MHz), the envelope of the received signal is digitized at 4 MHz and 128 signal samples centered around the transducer focal area are used to form the standard M-mode display where the amplitude of bubbles echoes are shown as a function of depth and time. As visible in Fig 1, each microbubble produces a corresponding trace, whose slope and brightness depend for a transmitted frequency on the measurable local US intensity, as well as on the bubble dimensions and composition. The observation of the M-mode images shows that the various traces can appear discontinuous, with variable width and multiple crossings. This can be explained by the bubble characteristics and by their mutual interaction. Moreover, the background of the images exhibits a large number of low intensity traces corresponding to not resonating bubbles or bubbles outside of the ultrasound focalized beam axis. As an example the brightest trace in Figure 1 indicates that one bubble with high reflectivity (probably close to resonance) travels the range 16-32 mm in about 1.9s.

B. Preprocessing

An image preprocessing step is applied to the original Mmode image to obtain continuous traces and to keep only the main traces in view to build a binary image. The M-mode images are acquired with a very large time resolution (1ms). An under-sampling is performed in the horizontal direction (perpendicular to the ultrasound propagation direction) by keeping, at a given depth, the highest grey level among 64 consecutive values. This processing reduces the intensity variation of the traces. Then to eliminate the noise in the background of the image, a threshold is determine as the median gray level value in the whole image and the pixels which gray level is below this threshold are set to zero. Local maxima in the vertical and diagonal directions are then detected using a mask of size 3x1 pixels and the two resulting images are combined by an logical OR function to provide a binarized image of the pixels that potentially belong to a trace (figure 2).



Figure 1: Undersampled Time Motion image of Microbubbles traces. The vertical axis reports the distance from US transducer



Figure 2 : Binary image given by the pre-processing step. It returns the skeleton of the traces.

C. Kalman filter

Kalman filtering is an iterative algorithm that allows to estimate the current value of variables such as the target position, velocity and acceleration, in a discrete time process, [4] [5]. Each estimate is performed using a prediction model based on the previous detected values and on the actual local measurements.

1) Filter implementation

Bubbles position is modeled by the kinematics equations

$$v = \frac{dx}{dt}; a = \frac{dv}{dt}$$
 (1)

Where x, v and a are the bubble position, velocity and acceleration respectively.

The values of acceleration, velocity and position at each time can be predicted from the equations (1). The evaluation involves a Singer model which defines the variable by its statistical properties [5]. By iterating the algorithm, a sequence of successive points corresponding to the bubble position at each time step is detected. Acceleration is assumed to be a centered random variable uniformly distributed between $-A_{max}$ and A_{max} , and its autocorrelation function is

$$\varphi(\tau) = \sigma_a^2 e^{-\lambda|\tau|} \tag{2}$$

where $\sigma_a^2 = \frac{A_{\text{max}}^2}{3}$ is the variance of acceleration and

 λ a parameter of maneuverability.

Kalman filter equations are:

$$X_{t+1} = \Phi X_t + G w_t \qquad (3)$$
$$x_t = H X_t + r_t \qquad (4)$$

where :

$$X_{t} = \begin{pmatrix} x_{t} \\ v_{t} \\ a_{t} \end{pmatrix} \qquad \Phi = \begin{pmatrix} 1 & T & 0 \\ 0 & 1 & T \\ 0 & 0 & e^{-\lambda T} \end{pmatrix}$$
$$Gw_{t} = \begin{pmatrix} 0 \\ 0 \\ w_{t} \end{pmatrix} \qquad H = \begin{pmatrix} 1 & 0 & 0 \end{pmatrix}$$

 X_t are the variables of the model, Φ is the matrix of dynamic system and T is the time step.

 Gw_t is the process noise; H is the measurement matrix, w_t a random gaussian noise, z_t the measured point (depth at time

t) and r_t the gaussian measurement noise.

To correctly track each bubble, two points are calculated for each time step: the predicted point and the measured one. Pixel coordinates from the time-motion visualization represent bubble position by its depth as a function of time and correspond to the variable x_t in the discrete time model.

2) Predicted point (x^p)

The value of the predicted point \hat{X}_t^p is calculated according to equation 3 as follows :

$$x_{t}^{p} = x_{t-1}^{p} + Tv_{t}$$

$$v_{t}^{p} = v_{t-1}^{p} + Ta_{t}$$

$$a_{t}^{p} = ba_{t-1}^{p} + w_{t}$$

$$b = e^{-\lambda T}$$
(5)

3) Measured point (x^m)

The measured point x_t^m is the closest pixel to the predicted one in the binary image.

4) Estimated point

The new position is deduced using the Kalman filter formula (equation 3) by considering the predicted value \hat{X}_t^p and the measured point values x_t^m :

$$X_{t}^{m} = \hat{X}_{t}^{p} + K_{t} \left(x_{t}^{p} - x_{t}^{m} \right)$$
(6)
$$K_{t} = P(t|t-1)H_{t}^{T} \left[H_{t} P(t|t-1)H_{t}^{T} + r_{t} \right]^{-1}$$
(7)

where P(t|t-1) is the covariance matrix of the estimated error of measurements.

$$P_{2|1} = \begin{pmatrix} \sigma_r^2 & \frac{\sigma_r^2}{T} & 0\\ \frac{\sigma_r^2}{T} & 2\frac{\sigma_r^2}{T^2} & 0\\ 0 & 0 & \sigma_a^2 \end{pmatrix}$$

 $P_{2|1}$ is the covariance matrix of the estimated error for the first pixel

 σ_r^2 is the variance of measure noise.

D. Filter initialization

For each trace, two points x_1 and x_2 are required to initialize the value of x and v in the filtering process. The acceleration a. is initialized to zero.

The first point x_1 is chosen from the gray level image and

corresponds to the pixel of maximal intensity from the first column (first signal). Whether this intensity is too low (inferior to a fixed threshold), this point should be extracted from the second column and so on. Then the second point

 x_2 is the one having the largest grey level among the neighboring pixels in the next column.

E. Control parameters

By setting adequately three parameters in the previous equations (3, 4) the range of the possible solutions could be constraint. The following values were defined experimentally to be suited to the shape of all the observed traces.

$$A_{max} = \frac{0.32}{T^2}, \text{ acceleration range}$$
$$\lambda = -\frac{\ln 0.7}{T}, \text{ filter maneuverability, (b=0.7)}$$
$$\sigma_r^2 = 1, \text{ variance of measure noise}$$

 A_{max} sets the range of acceleration values. A high value of A_{max} allows faster direction changing but also induces more oscillations around the solution before stabilization.

 λ represents the filter maneuverability, i.e. the weight accorded to the previous measurements. It physically represents the inertia of the system. A high value of λ sets a weak influence of the previous points in the estimation. Conversely a small λ forces the system to be less sensible to the direction changes.

The variance of the measured noise r represents the certitude granted to the measured point. This parameter sets the weight of the predicted point against the measured one in the choice of the new point.

F. Trace end criterion

In presence of a trace sudden interruption (due to bubble rupture), or disappearance of a trace (due to bubble movement away from focal area), a criterion is defined to stop the bubble tracking. The trajectory stops as far as n consecutive points have lower intensity than a threshold. The range of the values of n is empirically set between 2 and 5 pixels.

G. Post processing tests

Trajectories are finally smoothed through suitable low pass filtering. Then, the trajectories undergo two tests. The former one checks that velocity is positive, verifying that the trace is always descending. The latter one cancels a trajectory if it's too close to another, in order to avoid the double detection of a trace previously detected. Practically, two detected traces are considered as being the same, if they share more than 10 points.

III. RESULTS

A. Bubble tracking on simulated images

The accuracy of the method has been qualitatively and quantitatively evaluated on artificial images simulating different phenomena: trace crossings, intensity variations, sudden interruption and background noise. The final image resolution (after decimation in the pre-processing step) is 128 x 128 pixels.

The synthesized trace shapes are described by a polynomial equation P of an order 3. The artificial images are smoothed by a 3x3 mean filter to obtain more realistic images with larger traces.

After the application of the Kalman algorithm, a polynomial

curve P interpolating the detected point in a least-square sense is calculated. The maximum distance, the mean and the variance between the estimated and the reference shape are calculated as follows:

$$\max \ error = \max_{t} \left| P(t) - \hat{P}(t) \right|$$
$$mean \ error = mean_{t} \left| P(t) - \hat{P}(t) \right|$$
$$std \ error = \sqrt{\operatorname{var}_{t} \left| P(t) - \hat{P}(t) \right|}$$

The same set of tuning parameters is used for all the tests described below. The results are summarized in table 1

1) Intensity oscillation

When a bubble moves out of the focal zone, its intensity decreases. To simulate this effect, the intensity of the bubble is modulated according to its position. For example, the pixel intensity can become lower and some trajectories can even be temporarily interrupted. The maximum error remains lower than 1 pixel.

2) Adding noise on images

Acquired images are often noisy. This phenomenon is sometimes due to the weak echoes sent by the bubbles lying far from the center of the focal beam. Thus, the artificial images are simulated by adding a zero mean gaussian noise of standard deviation σ =2. The maximum error is lower than 2 pixels.

3) Trajectory crossing

The algorithm recognizes the 3 traces that follow exactly the reference ones. (figure 3)

4) Bubble rupture

The bubble rupture happens when it is submitted to a strong acoustic pressure. The trace stops suddenly. The stop criterion is well adapted because the algorithm stops the detection at the end of the trace.

An example of shape tracking in presence of trajectory crossing and bubble rupture is shown in figure 3.



figure 3 : bubble tracking on a simulated image with traces crossing and sudden trace interruptions)

	Max error	Mean error	Std error
	[pixels]	[pixels]	[pixels]
single trace	0.49	0.06	0.03
Intensity	0.59	0.08	0.04
oscillations			
Noised image	1.87	0.09	0.26
Trajectory	0.69	0.22	0.05
crossing			
Bubble rupture	0.45	0.12	0.03

Table 1 summarizes the distances (in pixels) between the measured trace and the reference one. The ideal case of a single trace of uniform brightness is reported as a reference.

B. Bubble tracking on experimental images

Several images have been acquired while using different US pressures and frequencies. Each image shows various trace behaviors..

Traces characterized by interruptions and crossing problems are illustrated in figure 4 where a bubble intersection appears in the middle of the image.



figure 4 : detection of trajectories on an image with bubble trace intersection

The figure 5 and 6 illustrate the influence the parameters of the model. The detection is performed on figure 5 with a maximal acceleration value which is less than the actual value. Figure 6 shows that a correct detection can be obtained with adapted parameter. A set of default values leading to satisfying results on almost all the processed images has been determined. A correct bubble tracking is obtained when the acceleration and the maneuverability are set in a range compatible with the actual value and in accordance with the under-sampling step related to the value of T.



figure 5 : detection of bubbles with sudden changes in direction. Bubble detection method applied with T=64ms leading to A_{max} =3.1 cm/s²



figure 6 : Same image as in figure 5 with a bubble detection method applied with a lower sampling step T=28ms and $A_{max}=16 \text{ cm/s}^2$.

Finally, the phenomenon of bubble rupture is visible in the center of the figure 7. As expected, the detection stops with rupture. The implemented algorithm is shown suitable to track the traces in almost all cases.



figure 7 : detection of trajectories on an image with many traces, and a rupture

IV. CONCLUSION

This paper presents a method to investigate the behavior of single microbubbles by tracking the corresponding traces produced in M-mode images. The proposed method based on Kalman filtering and Singer model makes possible to extract from the M-mode image most of the bubble traces even in presence of crossing, changing of intensity, sudden interruption and different noise levels. Two control parameters of the algorithm, the variance of acceleration and the maneuverability allow to obtain good trajectory detection in almost all the cases. Each recognized trace gives instantaneous velocity information. Comparison between these experimental data and the prediction of an appropriate simulation model could be used to estimate bubble physical properties like the diameter or the shell viscoelasticity.

V. .REFERENCES

- [1] [1] Chin CT, Lance'e C, Borsboom J, et al. Brandaris 128: A 25 million frames per second digital camera with 128 highly sensitive frames. Rev Sci Instru 2003;74(12):5026–5034.
- [2] F. Guidi, E. Boni, P.Tortoli, "Acoustic Method for Real-Time Visualization of Microbubbles Movements and Rupture", IEEE Ultrasonics Symposium, 2003. Volume 2, 5-8 Oct. 2003 Page(s):1183 - 1186
- [3] P.Tortoli, M.Pratesi and V.Michelassi "Doppler Spectra from Contrast Agents Crossing an Ultrasound Field", IEEE Trans. on Ultrason., Ferroelect., Freq.Contr., vol.47, n.3, pp.716-725, 2000.
- [4] P.S. Maybeck, "Stochastic Models, Estimation and Control" Vol 1, Academic press, 1979
- [5] G. Welch, G. Bishop, "An introduction to the KalmanFilter" Technical Report No. TR 95-041, Department of Computer Science, University of North Carolina, March 2003.