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Nonlinear modeling of ultrasound contrast agents with Wiener series

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ABSTRACT:

The use of ultrasound contrast agents has been widespread in clinical echography. Since they consist of highly compressible gas microbubbles, they are ideal markers for perfusion. To predict their dynamic behaviour under ultrasound insonification, oscillation models have been developed. Current models used for the prediction of the dynamic behaviour are implemented by nonlinear differential equations. The determination of the coefficients of these differential equations is problematic because they need to be determined individually per agent per bubble size.

This paper introduces ultrasound contrast agent modelling by Wiener series. To conduct the identification, a simulated contrast agent, described by a Rayleigh-Plesset model, is insonified with white noise. The resulting output is used for identification of the Wiener kernels.

The Wiener model allows for an estimation of the bubble movement with a mean square error of 7.1% in relation to the reference signal.

INTRODUCTION:

Ultrasound contrast agents consist of microbubbles with diameters in the μm range encapsulated by a shell. To model the dynamic behaviour under ultrasound insonification, oscillation models, such as the Rayleigh-Plesset model, have been developed. This model has been implemented by a nonlinear differential equation. To account for the influence of the shell, the model has been extended with shell parameters such as shell stiffness, or shell friction.

The determination of the parameters of such a model, however, is problematic since they cannot be determined from the physical properties of the materials used for manufacture.

To overcome this drawback, a system theoretical approach is taken. Since a contrast agent can be considered a nonlinear system, nonlinear system theory can be applied to develop and identify a model for ultrasound contrast agents.

METHODS:

The output $y(n)$ of a nonlinear system with input $x(n)$ can be described by a Wiener series [1]:

$$y(n) = \sum_i G_i[h_i(k_1, \dots, k_i); x(n)], \quad (1)$$

with G_i denoting the Wiener operators with

$$G_i = \sum_{k_1} \dots \sum_{k_i} h_i(k_1, \dots, k_i) x(n - k_1) \dots x(n - k_i). \quad (2)$$

These are chosen to be mutually orthogonal such that

$$E G_i G_j = \begin{cases} 0, & i \neq j \\ c, & i = j, c > 0 \end{cases} \quad (3)$$

with E denoting expectation. The behaviour of the system is defined by the Wiener kernels h_n . These were determined with an efficient and numerically stable orthogonal search algorithm [2].

To test the performance of the identification approach, a contrast agent was simulated by the modified Rayleigh-Plesset model. Band-limited white noise was used as the input signal. The output was recorded and input and output were used for identification of model parameters.

RESULTS:

The linear, square and cubic Wiener kernels obtained by identification from a simulated microbubble are shown in Figures 1, 3 and 4.

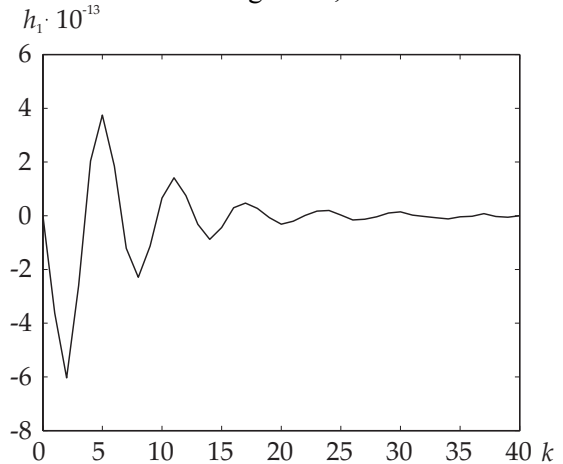


Figure 1: Linear kernel h_1 .

In the linear kernel, the conventional linear impulse response of the microbubble can be seen. Clearly, it shows the characteristics of a damped oscillator. Furthermore, if all nonlinear components were considered negligible, the linear frequency response of a microbubble could be obtained from the linear kernel as shown in Figure 2.

Band pass behaviour can be observed with a centre frequency of 6 MHz.

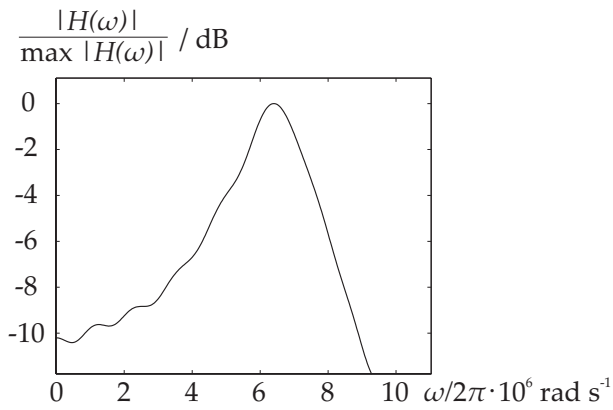


Figure 2: Spectrum obtained from linear kernel h_1 .

The quadratic and cubic kernels are displayed in Figures 3 and 4. The temporal memory of the nonlinear system can be determined by evaluating these kernels. Furthermore, the threshold for nonlinear oscillation can be determined from the amplitude of the quadratic and cubic kernels.

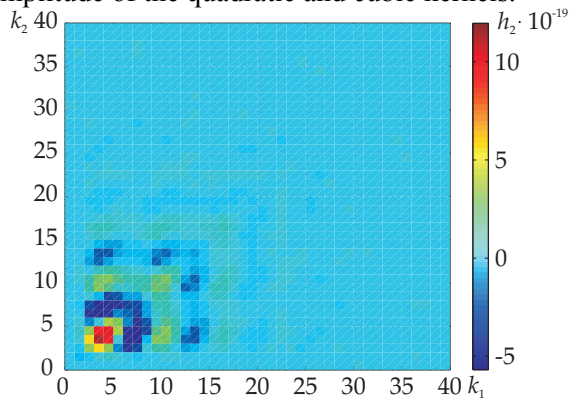


Figure 3: Quadratic kernel h_2 .

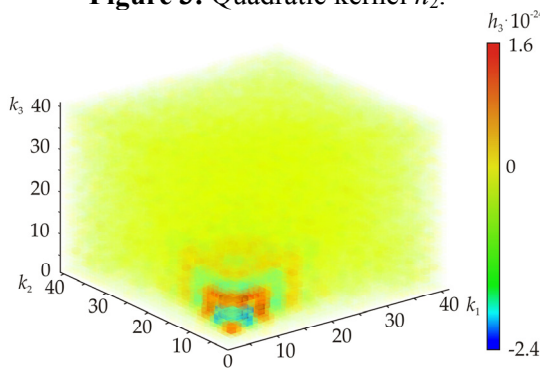


Figure 4: Cubic kernel h_3 .

The estimate of bubble oscillation obtained by solving (1) for a sinusoidal input is shown in Figure 5. For reference, the output from the modified Rayleigh-Plesset model used for identification is plotted for the same input.

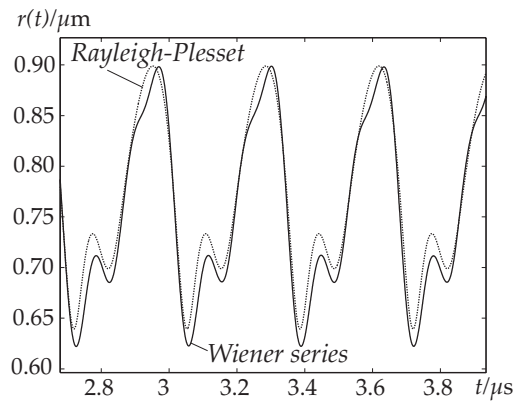


Figure 5: Bubble excursion obtained by numerically solving modified Rayleigh-Plesset equation (dotted line) and approximated by the Wiener series (solid line) (acoustic amplitude of excitation $p=100$ kPa, driving frequency $f=3.0$ MHz, bubble diameter $r_0=0.75$ μm).

DISCUSSION:

The quality of estimation attained by the Wiener model can be judged from Figure 5 and gives an RMS error of 7.1% in respect to the power of the reference signal. There are slight deviations to curve progression which are due to the fact that not all nonlinear components of the Rayleigh-Plesset model are considered. However, the simulation demonstrates the applicability of the identification approach to contrast agent modelling.

Furthermore, details on contrast agent behaviour under ultrasound insonification can be deduced from the identified Wiener kernels. For instance, the acoustic pressure necessary for nonlinear oscillation can be determined by evaluation of square and cubic Wiener kernel amplitude.

CONCLUSIONS:

It was shown that modelling of ultrasound contrast agents with Wiener series is feasible. In simulations conducted to assert the results, performance of the new model was verified by comparison with the simulated microbubble. The curves obtained are in agreement.

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