Chapter 3

Crawling wave sonoelastography

Crawling Wave Sonoelastography (CrWS) is an elasticity imaging technique which was recently proposed by Wu et al. [18,19]. In this technique, two opposing shear wave vibration sources are vibrated at slightly offset frequencies producing a slowly propagating interference pattern, termed Crawling Waves (CrW). Sonoelastography (see Chapter 2) is used to visualize the CrW in real time. The apparent velocity of the CrW is proportional to the underlying shear velocity of the tissue, and can be used to estimate locally its elasticity modulus. The main advantage of this technique is that it offers a quantitative estimation of the viscoelastic properties of the tissue. In this chapter, the theory behind this imaging technique will be reviewed. Additionally, image processing techniques to improve the quality of the CrW are proposed as well as shear velocity estimators to extract elasticity information from the images.
3.1 Interference patterns and crawling waves

Wu and colleagues proposed the experimental setup described in Figure 3.1 to image the shear wave interference pattern created by two external sources using sonoelastography. Two piezoelectric devices are used as vibration sources and are driven at identical frequencies and amplitudes. The two sources are placed opposing each other and their tips oscillate along a vector parallel to the lateral surface of the sample. The shear waves produced by the sources interfere with each other and are imaged by the transducer sitting on top of the sample. Since sonoelastography only images the particle motion along the ultrasound beam, only the $y$ component of the wave motion is discussed.

Under the plane wave assumption and considering a homogenous sample, the shear waves introduced by the right and left vibration sources can be described as follows:

$$ W_{right} = e^{-\alpha(x+D/2)}e^{-i(k_1(x+D/2)-w_1t)} $$ (3.1)

$$ W_{left} = e^{-\alpha(D/2-x)}e^{-i(k_2(D/2-x)-w_2t)} $$ (3.2)

where $\alpha$ is related to the attenuation of the wave in the sample, $D$ is the distance between the sources, $k_1$ and $k_2$ are the wave numbers and $w_1$ and $w_2$ are the frequencies of the vibration sources. In this particular case $w=w_1=w_2$ and $k=k_1=k_2$. 
Figure 3.1. Experimental setup for the visualization of shear wave interference patterns using Sonoelastography. Two external mechanical sources (a), in contact with the testing sample (b), vibrate in the direction perpendicular to the ultrasound probe (c).

The resulting pattern is the superposition of the two waves. The squared signal envelope will result in:

\[ |u(x,t)|^2 = (W_{\text{right}} + W_{\text{left}})(W_{\text{right}}^* + W_{\text{left}}^*) \]  \hspace{1cm} (3.3)

\[ |u(x,t)|^2 = e^{(-\alpha D)}[e^{2\alpha x} + e^{-2\alpha x} + e^{2ix} + e^{-2ix}] \]  \hspace{1cm} (3.4)

\[ |u(x,t)|^2 = 2e^{(-\alpha D)}[\cosh(2\alpha x) + \cos(2kx)] \]  \hspace{1cm} (3.5)

The interference patterns described in Equation 3.5 depend on a hyperbolic cosine and a cosine term. In the central region and under weak attenuation, the hyperbolic
cosine term becomes approximately constant. Under such consideration, the spatial frequency of the interference patterns becomes $2k$. Thus, the interference fringe spacing is half the intrinsic shear wave wavelength ($\lambda$).

The shear wave velocity is estimated as:

$$V_{\text{shear}} = f \cdot \lambda$$  \hspace{1cm} (3.6)

where $f$ is controlled and given by the vibration sources and $\lambda$ is measured from the image. In soft tissue, the relationship between Young’s modulus and shear wave velocity can be approximated as follows:

$$E = 3 \rho (V_{\text{shear}})^2$$  \hspace{1cm} (3.7)

where $\rho$ is the mass density and considered to be approximately 1 g/mL.

If there is a slight difference in frequency between the vibration sources, the interference patterns will slowly move towards the source with lower frequency. As mentioned previously, these moving patterns were termed “Crawling Waves” [18,19]. The advantage of having CrW is that they give more observations from which to estimate the shear velocity of the sample. Problems due to tissue attenuation and small region of interest (as compared to the shear wave wavelength) can be overcome using CrW as opposed to having static interference patterns.

By introducing a slight offset between the vibration sources ($k_1 = k$, $k_2 = k + \Delta k$, $w_1 = w$, $w_2 = w + \Delta w$), Equation 3.5 is transformed into:
\[
\mu(x,t)^2 = 2 \exp(-\alpha D) \left[ \cosh(2\alpha x) + \cos(2kx + \Delta kx + \Delta wt) \right]
\] (3.8)

Note that the cosine term also depends on the time variable.

### 3.2 Generation of crawling waves

The crawling wave phenomenon depends on two external mechanical sources opposing each other to produce shear vibration and create the interference patterns.

The original experimental setup proposed by Wu et al. [18,19] relied on piezoelectrics (bimorph, Piezo Systems, Cambridge, MA, USA) as point sources to generate the CrWs (see Figure 3.2a). Further studies [24] demonstrated that shear line sources can also be applied. The line sources were surface-abraded extensions which were fitted to a piston-type vibration source. This experimental setup is well fitted for 	extit{ex vivo} tissue imaging, but may not be suitable for clinical applications.

To overcome this problem, Hoyt and colleagues [26,27] proposed the utilization of normal line sources applied on the surface of the tissue (see Figure 3.3a). Using this experimental setup, the plane wave assumption described in the previous section is not valid. By following a mechanical model [88], which describes the field emitted by mechanical radiators in free surfaces, they realized that there is a region of interest in the image in which the plane wave assumption is valid (see Figure 3.3a). This analysis was verified by experimental results (see Figure 3.3b).
Even though, CrW can be generated by several methods, its dependence on external mechanical sources is still an important drawback for this imaging technique. Currently, research is underway to create CrW using acoustic radiation force. [89]

### 3.3 Shear velocity estimation

An important step to obtain relevant clinical information from CrW is the estimation of the underlying shear velocity. Local frequency estimators (LFE) were initially proposed by Wu et al. [18,19] to perform this task since they were already being applied successfully to MRE images. A disadvantage of this technique when applied to CrW imaging is that it requires amplitude normalization and detrending to avoid
degradation in the estimation. An alternative method was proposed by McLaughlin et al. [22]. In this approach, salient features of the CrW and arrival times at points in the image plane are used to calculate the local shear velocity distribution in the image. A major drawback of this approach is the required computational complexity which does not allow a real-time implementation.

Figure 3.3. Scheme of the experimental setup to generate crawling waves using normal line sources (a), and a CrW image of an homogenous phantom extracted from the region of interest as marked in (a).
In this section, two algorithms to estimate the viscoelastic properties of tissue are presented. First, a correlation algorithm to calculate the viscoelastic properties of homogeneous tissue is introduced. Subsequently, an autocorrelation algorithm, capable of mapping local estimations of the shear velocity into an image, is presented.

### 3.3.1 Correlation algorithm

In clinical applications such as liver fibrosis staging or assessment of skeletal muscle functioning, it is not required to obtain an image representing the local distribution of the elastic properties of the tissue, but rather obtain an average value of the elasticity of the overall imaged sample. The proposed algorithm combines the information of a region of interest in order to obtain a robust estimate of the overall elasticity.

The algorithm requires that the user inputs a region of interest (ROI) which is far from the vibration sources. Under this consideration, the interference patterns in the ROI appear as parallel stripes (see Figure 3.4a). A projection of the image over the axis perpendicular to the stripes is built and fit into a cosine model (see Figure 3.4b):

\[
Y = A \cos(2\pi k_s X - \theta) + D
\]  

(3.9)

where \(Y\) is the projection built from the ROI; \(A, k_s, \theta, D\) are the parameters of the model: Amplitude, spatial frequency, phase and offset respectively; and \(X\) is the independent spatial variable. Note that \(k_s = 1/\lambda_s\).
Figure 3.4. Crawling wave image (a) showing the region of interest selected by the user (red box). A projection is built from the region of interest and fit into a cosine model (b).

This curve-fitting process is repeated for all the observations (i.e. each frame in the CrW movie). The final step is a cross optimization process performed over all observations. The estimated parameter ($k_s$) is used to calculate the shear wave velocity and hence, the elasticity modulus:

$$V_{\text{shear}} = \frac{2f}{(1000)(k_s)(\text{pixel}_\text{mm})}$$  \hspace{1cm} (3.10)

where $f$ is the external vibration frequency and $\text{pixel}_\text{mm}$ is the conversion factor from $\text{mm}$ to $\text{pixels}$.
The proposed algorithm was employed to calculate the viscoelastic properties of a human prostate gland \textit{ex vivo} [25] (see Figure 3.5a). The estimations agreed with results from mechanical measurements using a Kelvin-Voigt Fractional Derivative model [13].

Figure 3.5. Crawling waves propagate through the region of interest in a human prostate gland (a); a comparison of the viscoelastic properties calculated with CrWS and mechanical measurements taken from core sample of the gland (b).

\subsection*{3.3.2 Local autocorrelation algorithm}

In other clinical applications such as prostate or breast cancer detection, it is important to establish the size and boundaries of the tumors, and therefore, an image is required. A real-time estimator has been proposed by Hoyt \textit{et al.} [23,24] based on autocorrelation methods [86,87]. One of the main advantages of this method is its
computational simplicity, comparable to current color flow processing available in commercial US scanners.

In this approach, a support kernel –a window inside the image of a pre-determined size $M$ by $N$ (e.g. 20 x 20 pixels)– is used to estimate the local shear velocity. For that purpose, the Hilbert transform is used to create an analytical image from the original CrW image. The discrete analytic image $\hat{u}(m,n)$ of the CrW image $u(m,n)$ is defined as:

$$ \hat{u}(m,n) = u(m,n) - j\tilde{u}(m,n) $$ (3.11)

where $\tilde{u}(m,n)$ denotes the discrete 1D Hilbert transform of $u(m,n)$ along the $n$-axis

and:

$$ \tilde{u}(m,n) = \frac{-1}{\pi n} u(m,n) $$ (3.12)

Assuming that the CrW are moving along the $n$-axis, the shear velocity in that direction can be estimated by evaluating the phase of the two-dimensional autocorrelation function $\gamma(m',n')$ of the analytic signal $\hat{u}(m,n)$ at lag $(m' = 0, n' = 1)$ and where $*$ denotes the complex conjugation operator:

$$ \tilde{\gamma}(m',n') = \sum_{m=0}^{M-m'-1} \sum_{n=0}^{N-n'-1} \hat{u}^*(m,n)\hat{u}(m+m',n+n') $$ (3.13)
The shear velocity along the n-axis ($<v_s>_n$) is finally computed as:

$$<v_s>_n = \frac{2\pi(2f_s + \Delta f_s)T_n}{\tan^{-1}\left[ \frac{\text{Im}\{\gamma(0,1)\}}{\text{Re}\{\gamma(0,1)\}} \right]}$$

(3.14)

Where $f_s$ is the vibration frequency, $\Delta f_s$ is the offset in frequency between the two vibration sources, and $T_n$ is the spatial spacing in the $n$-axis. All these parameters are known.

In a similar fashion, the shear velocity along the m-axis ($<v_s>_m$) is computed as:

$$<v_s>_m = \frac{2\pi(2f_s + \Delta f_s)T_m}{\tan^{-1}\left[ \frac{\text{Im}\{\gamma(1,0)\}}{\text{Re}\{\gamma(1,0)\}} \right]}$$

(3.15)

where $T_m$ is the spatial spacing in the $m$-axis.

In an ideal situation, the CrW are moving along the n-axis, and therefore, the estimation of the shear velocity in that direction should be enough to describe the viscoelastic properties of the tissue. In practice, boundary conditions or slight misplacements in the experimental setup change the direction of the CrW. Therefore, estimation of the shear velocity in the $m$-axis direction is required. Both estimations can be combined to obtain a single and more accurate estimate of the shear velocity of the sample, which was named a two-dimensional shear velocity estimate ($<v_s>_{2D}$).
By understanding the geometrical relationship among ($v_s > m$), ($v_s > n$), and ($v_s > 2D$), an angular component $\theta$ (see Figure 3.6.) can be defined as:

$$\theta = \tan^{-1}\left(\frac{\langle v_s \rangle_m}{\langle v_s \rangle_n}\right)$$

(3.16)

Figure 3.6 Two-dimensional description of the mean shear velocity vectors in relation to a representative shear wave interference pattern. Note that local increases in shear wavelength (for a fixed vibration frequency) correspond to local increases in shear velocity values. The two-dimensional shear velocity estimate is represented by the red arrow.

The two-dimensional shear velocity estimate ($v_s > 2D$) can be defined as:

$$\langle v_s \rangle_{2D} = \langle v_s \rangle_n \sin \theta$$

(3.17)

Using some trigonometric identities, Equation 3.17 can be rewritten as:
\[
\langle v_s \rangle_{2D} = \frac{\langle v_s \rangle_m}{\left(\langle v_s \rangle_m \right)^2 + 1}
\]  
(3.18)

Since Equation 3.18 produces a local shear velocity estimate, 2D spatial distributions are obtained by shifting the support kernel one sample throughout the CrW image. The result is an image which represents the local shear velocity of the tissue which is termed shear velocity sonoelastogram. Examples of shear velocity sonoelastograms are shown in Figure 3.7b and Figure 3.8b for homogenous and inclusion phantoms.

Figure 3.7. Crawling wave image (a) and its corresponding shear velocity sonoelastogram (b) of a homogenous phantom. The shear velocity was estimated as 2.73 m/s using the local autocorrelation approach, which agrees with time of flight measurements (2.75 m/s).
Figure 3.8. Crawling wave image (a) and its corresponding shear velocity sonoelastogram (b) of an inclusion phantom. The 5mm-diameter inclusion is depicted clearly in the shear velocity sonoelastogram. The inclusion was approximately 3 times harder than the background.

3.4 Enhancement of crawling wave images

The accuracy of the estimation of the shear velocity spatial distribution depends on the quality of the crawling waves. Previously, pre-processing schemes have focused on improving the spatial characteristics of a single CrW image. In [23], the first two Fourier series coefficients were suppressed when computing the analytic image to compensate for the hyperbolic cosine shape that is expected in a CrW image. This
approach was combined with standard techniques such as median filtering and amplitude normalization.

This section introduces a pre-processing scheme to enhance the quality of the CrW images by taking into account the time relationship among the frames of a CrW movie (cine loop) imaging the same spatial location. An additional advantage of this processing is the generation of a quality metric which can be used to discriminate the shear velocity information accordingly.

Figure 3.9 summarizes the proposed approach. A CrW movie is taken at a single position in the tissue. Each frame of the movie is processed using a median filter to reduce the noise. Due to the nature of CrW imaging, the median filter uses a support kernel which is longer than wider (e.g. [7x3]). Subsequently, the images are improved by 4 processes: Horizontal and vertical motion filtering, slow time filtering and a phase multiplication.

3.4.1 Motion filtering

Two types of motion filtering are applied to the data. First, a horizontal motion filter [119] is applied to improve SNR and reduce potential reflection artifacts. A horizontal line from the CrW movie (blue line in Figure 3.10a) is followed in time to form a 2D image which would ideally look like Figure 3.10c. The 2D Fourier transform of such an image would have its energy concentrated in two peaks
(sinusoidal in time and space) of known frequencies since the speed of the CrW and the Doppler frame rate are controlled. A band-pass filter (Figure 3.10d) is applied to reduce noise and artifacts. This operation is repeated for all the lines in the CrW movie. Similarly, a vertical motion filter is applied. In this case, a vertical line is followed in time to form an image, and a low-pass filter is employed since most of the energy is concentrated in the time axis.

Figure 3.9. Proposed scheme to enhance the crawling wave images.
Figure 3.10. Slow-Time and Motion Filters. The slow time signal at each pixel of the crawling wave movie (red line in (a)) is replaced with its sinusoidal version. The original signal and its sinusoidal correction are plotted in (b) in blue and red colors, respectively. (c) shows an image representing the evolution of a single line in the CrW movie (blue line in (a)), and (d) presents a band pass filter used for motion filtering.
3.4.2 Slow time filtering

The slow time filter processes the signal obtained from a single spatial position (i.e. pixel) in time. Since the CrW are governed by Equation 3.8, the magnitude of the signal in each position should vary following a sinusoidal pattern with frequency equal to $\Delta f$. The slow time signals are then fit into a sinusoidal model:

$$Y = A \cos(2\pi \Delta f X + \theta) + D \quad (3.19)$$

where $Y$ is the value of the slow time signal, and $X$ is the independent value which corresponds to the frame number. $A$, $\theta$, and $D$ are the parameters of the model to be estimated and correspond to the amplitude, phase, and offset of the signal, respectively.

Since this optimization process could be time consuming and computationally expensive, the parameters are initialized as follows: $A$ is initialized to half the difference between the maximum and the minimum value of the slow time series, $D$ is initialized to the mean value of the signal, and $\theta$ is initialized using the result of a cross-correlation process between the slow time signal and a normalized cosine. It is important to note that this processing requires that the slow time signal should contain data corresponding to at least 75% of a full cycle, so as to ensure the maximum and minimum values are captured.
Two images are obtained as a result of the slow time processing: A phase image and an $r^2$-value image. From the phase image, a filtered version of the CrW movie can be reconstructed. In this filtered version, the CrW have normalized amplitude and noise effects have been considerably reduced. The $r^2$-value image represents the goodness of fit in the optimization process for each of the pixels of the CrW image. This image can be employed as a quality index of the CrW movie. Figure 3.11 shows a simulation of CrW images before and after slow time filtering. Examples of phase and $r^2$-value images for the same CrW movie are given in Figure 3.12.

### 3.4.3 Phase multiplication

In order to improve the estimation of shear velocity using the autocorrelation approach (See Section 3.3.2), the phase image is multiplied by a factor (*i.e.* four) before reproducing the CrW images. As a consequence, the final processed CrW movie has four times the spatial frequency than its original version. The autocorrelation process is equivalent to finding the mean frequency of the spectrum. Due to the relative small size of the kernel (used for estimation) when compared to the wavelength of the signal, the mean frequency is usually between the first and second coefficients of the spectrum. By artificially increasing the spatial frequency of the signal, the estimator is given a larger range to estimate the mean frequency. Figure 3.13 illustrates the concept of phase multiplication in one dimension. Figure 3.13a shows the signal in space before (red) and after (blue) phase multiplication. It can be observed that the spectrum is shifted to higher frequencies after phase
multiplication (Figure 3.13b). The multiplication factor of four was selected after analyzing a few CrW movies in *ex vivo* prostate glands. Given the expected shear velocity of the tissue and the range of vibration frequencies used (100 – 140 Hz), the factor of four gave the estimator a larger range for estimation without having problems of aliasing. This factor will need to vary for a different application.

![Figure 3.11](image)

**Figure 3.11.** Crawling waves before (a) and after (c) slow time filtering. Corresponding plots of the line at y=40 are shown in (b) and (d).
Figure 3.12. Phase (a) and $r^2$-value (b) images corresponding to the crawling wave images shown in Figure 3.11.

Figure 3.13. One dimensional plots representing the data observed by the kernel of the local autocorrelation estimator in (a) space and (b) spatial frequency. Signals before and after phase multiplication are plotted in red and blue, respectively.
3.4.4 Simulations

A CrW movie on a homogeneous media was simulated to test the performance of the motion filtering, slow time filtering and phase multiplication stages under the presence of noise and reflection artifacts. The movies simulated a CrW with shear velocity $= 3 \text{ m/s}$. Gaussian noise (SNR = 15dB) and 50% reflection were added to the images to imitate the conditions observed in the ultrasound scanner.

Figure 3.14 illustrates the results from the shear velocity estimator when applied (a) directly to the simulated CrW movie, (b) after slow-time filtering, and (c) after motion and slow time filtering. In the first case (a), the autocorrelation method failed to estimate the correct shear velocity in the presence of noise. In the second case (b), slow time filtering is able to improve the SNR of the CrW movie, but it is still susceptible to the presence of reflections which produce a ripple artifact in the estimation. The combination of motion and slow-time filtering (c) compensates for the noise and the reflection problems providing a more constant result.
Figure 3.14. Results from the shear velocity estimator applied directly to the simulated CrW movie (a), applied after slow time filtering (b), and applied after motion and slow time filtering (c). The CrW simulated a homogenous region with shear velocity $= 3 \text{ m/s}$.

Figure 3.15 presents the results from the shear velocity estimator (a) without and (b) with a phase multiplication of four applied to the same simulated movie. Estimations with the autocorrelation method were evaluated using several kernel sizes. The results after phase multiplication showed a more uniform estimation even when a smaller kernel size was used. There is a compromise in the selection of the kernel size for the autocorrelation estimator. Having a larger kernel provides estimations less susceptible to the starting phase of the signal but it reduces the field of view and smoothes the results. Phase multiplication, as shown in Figure 3.15b, permits estimation comparable to the findings without phase multiplication but with smaller kernel sizes.
Figure 3.15. Results from the shear velocity estimator (a) without and (b) with phase multiplication of four. The CrW were simulated in a homogenous region with shear velocity $= 3 \text{ m/s}$. The estimations were performed with kernel sizes of 30x30 (red), 25x25 (green), 20x20 (blue), 15x15 (black) and 10x10 (yellow). Estimations after phase multiplication show a more uniform behavior.

3.5 Summary

In this chapter, the foundations for Crawling Wave Sonoelastography were reviewed. The theory on the formation of shear wave interference patterns and their visualization with sonoelastography was presented. It was shown that crawling wave images can be generated with different experimental setups including shear and normal external vibration sources. Two correlation-based estimators were presented to extract shear velocity information from the images. Finally, the last section of the chapter discussed image processing techniques to enhance the quality of the images.
There are two main contributions in the current chapter. First, a correlation-based algorithm was proposed to extract shear velocity information from a homogenous tissue. This algorithm has been successfully applied to the measurement of viscoelastic properties of human prostate and veal liver tissues \textit{ex vivo} [25]. Second, a filtering approach (motion filtering and slow time processing) is proposed to enhance the quality of the CrW images by using the time relationship between frames in a CrW movie. As an additional advantage, the processing of the CrW movies generates a quality metric image which can be used to discard regions with poor signal to noise ratio in the image.

The following chapters of the thesis apply sonoelastography and crawling wave sonoelastography to prostate cancer detection and to the measurement of thermal ablated lesions \textit{ex vivo} and \textit{in vivo}. Image processing tools for these tasks are further developed.