Automated Ultrasonic Arterial Vibrometry: Detection and Measurement

Melani I. Plett\textsuperscript{a}, Kirk W. Beach\textsuperscript{b}, Marla Paun\textsuperscript{b}

\textsuperscript{a}Department of Engineering, Seattle Pacific Univ., Seattle, WA 98119

\textsuperscript{b}Univ. of Washington, Box 356410, Seattle, WA 98195

ABSTRACT

Since the invention of the stethoscope, the detection of vibrations and sounds from the body has been a touchstone of diagnosis. However, the method is limited to vibrations whose associated sounds transmit to the skin, with no means to determine the anatomic and physiological source of the vibrations save the cunning of the examiner.

Using ultrasound quadrature phase demodulation methods similar to those of ultrasonic color flow imaging, we have developed a system to detect and measure tissue vibrations with amplitude excursions as small as 30 nanometers. The system uses wavelet analysis for sensitive and specific detection, as well as measurement, of short duration vibrations amidst clutter and time-varying, colored noise. Vibration detection rates in ROC curves from simulated data predict > 99.5% detections with < 1% false alarms for signal to noise ratios $\geq 0.5$. Vibrations from \textit{in vivo} arterial stenoses and punctures have been studied. The results show that vibration durations vary from 10-150 ms, frequencies from 100-1000 Hz, and amplitudes from 30 nanometers to several microns.

By marking the location of vibration sources on ultrasound images, and using color to indicate amplitude, frequency or acoustic intensity, new diagnostic information is provided to aid disorder diagnosis and management.

Keywords: detection, hypothesis testing, estimation, adaptive, non-stationary, wavelets, vibrations, ultrasound, arteries

1. INTRODUCTION

For centuries, clinicians have been listening to the human body as a means to detect and diagnose cardiovascular disorders. In 1816, René Laennec dignified this technique with the invention of the stethoscope\textsuperscript{8}. Today, auscultation with a stethoscope has become routine. Clinicians are listening for sounds emanating from arteries (bruits) or from the heart (murmurs). These sounds indicate vibrations in the tissue, which are likely produced by disturbances in the blood flow. Such disturbances typically arise from stenoses, aneurysms and arterio-venous fistulas (see Figure 1), although some occur in the absence of a disorder\textsuperscript{2-13}. The sounds, which are used to detect a possible disorder, also aid in the diagnosis of the disorder type based on several characteristics of the sound, including: spatial location, temporal duration, timing in the heart cycle, frequency, loudness (intensity or amplitude), quality (sound character = frequency/bandwidth), and radiation (presence along a vessel). Typically these characteristics are recorded only qualitatively. When quantified, though, they will potentially provide insight into the significance and natural progression of the disorder, as well as the mechanism of vibration.

Quantification of arterial vibration parameters requires the ability to capture the vibration for subsequent analysis. To date, vibrations can be captured non-invasively at the skin surface with stethoscopes\textsuperscript{2-4,10} and microphones (phonoangiography\textsuperscript{11,12} and phonocardiography), and below the skin with conventional Doppler ultrasound\textsuperscript{13-17}. None of these methods has the ability to measure all of an arterial vibration’s characteristics at the site of the disorder below the skin surface. The stethoscope provides only qualitative aspects of vibrations that propagate to the skin surface with sufficient intensity to be discerned by the clinician. Also limited to vibrations that reach the skin surface, phonoangiography and phonocardiography involve time or frequency analysis of signals received by a microphone placed at the skin. These methods have succeeded in quantifying some, but not all, important vibration characteristics, causing them to have minimal advantage over the stethoscope. Phonoangiography and phonocardiography are therefore rarely used in the clinic. Doppler ultrasound, both pulsed and color, can examine regions below the skin surface. Current Doppler techniques, however, are highly dependent on system settings and do not promote effective vibration measurement. Finally, in their efforts to carry out sonoelasticity,
researchers have developed pulsed ultrasound methods to measure large, stationary, narrowband vibrations, usually with known frequencies\textsuperscript{18}. Since vibrations from arterial disorders are both small and transient, the methods designed for sonoelasticity do not apply to them. Because non-invasive techniques are not sufficient, researchers studying arterial disorders have developed invasive techniques that alter the region of interest and are only applied to animals\textsuperscript{5-8}. Thus, the research has been limited by the absence of a non-invasive means of completely quantifying arterial vibrations.

Figure 1. Illustration of arterial disorders.

The results from both the non-invasive and invasive studies do still provide valuable information for the design of a more effective non-invasive detection and measurement system. Qualitatively, the literature describes the vibrations as propagating from vessel walls with frequency bandwidths ranging from extremely narrowband to broadband. The signal-to-noise ratios range from imperceptible to obvious, varying with both the vibration itself and the measurement method employed. Pulsed Doppler displays of the vibrations indicate that strong, low frequency clutter is present, and the noise is both colored and non-stationary. Quantified characteristics available in the literature from naturally occurring vibrations are summarized in Table 1. The fact that a lot of effort has been made to understand and quantify these vibrations over the past thirty years underlines both their importance and the continued need for an efficient means of accomplishing this task.

Table 1. Vibration characteristics from the literature.

<table>
<thead>
<tr>
<th>Vibration characteristic</th>
<th>Minimum value</th>
<th>Maximum value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency (Hz)</td>
<td>100</td>
<td>1000</td>
</tr>
<tr>
<td>Quality factor</td>
<td>1 (broadband)</td>
<td>10 (narrowband)</td>
</tr>
<tr>
<td>Duration (ms)</td>
<td>Stenoses and aneurysms</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Cardiac vibrations and arterio-venous fistulas</td>
<td>NA</td>
</tr>
</tbody>
</table>

The long term goal is to develop an automatic, real time system to detect, measure and locate vibrations that arise from stenoses, aneurysms, arterio-venous shunts and bleeds. The system will obtain real-time vibrational amplitude, frequency, and duration measurements, as well as locate the vibration source spatially in the ultrasound image and temporally in the cardiac cycle. Analysis will be applied simultaneously to multiple spatial locations within a two dimensional region of the body (~ 10 cm\textsuperscript{2}). This will provide information about the spatial distribution of the vibrations, as well as fast, efficient detection and measurement of the vibration. Combined, this information will aid understanding, diagnosis, prognosis and management of the arterial disorder. For bleeds, the goal is to localize the bleeding site for subsequent transcutaneous cauterization with high intensity focused ultrasound (HIFU)\textsuperscript{19}. Regardless of the disorder type, the detected vibration parameters will be superimposed on a conventional ultrasound image for ease of interpretation. To minimize the efforts needed for commercial implementation and United States Food and Drug Administration (FDA) approval, the design will use
straightforward modifications to the transmit sequences of modern diagnostic ultrasound instruments. Currently, a one-dimensional, offline system is in place and the success of the system has been demonstrated in humans and animals.

The methods outlined here for arterial vibrometry have applications in the clinic, the biomedical research laboratory and the signal processing laboratory. For the clinician, the system developed here provides a sensitive, automatic detection and measurement method that will enhance diagnosis and treatment of arterial disorders that generate vibrations. The ability to non-invasively measure subcutaneous vibrations will also afford long-awaited measurements in the research of arterial disorders. From a signal processing perspective, this detection system expands existing wavelet detection methods to a class of signals where traditional detection methods fail: transient, oscillatory signals in additive Gaussian noise with unknown, non-stationary noise variance in low frequency clutter.

In addition to arterial disorders, other physiology can be studied with this technique with only slight modifications. For instance, muscle tremor, speech, respiration, and digestion are all known to produce similar vibrations. Furthermore, the vibration signals of interest here resemble signals that occur in other settings: underwater acoustics, radar, sonar, seismology and vibrating mechanical systems. Finally, if the temporal coordinate is replaced with an appropriate spatial coordinate, the analysis can also be applied to identifying transient periodic structures in images, provided the background noise has a Gaussian distribution.

2. METHODS

Detection and measurement of tissue vibrations require two steps: data collection and data analysis. The data to be collected are tissue displacements. Ultrasound is uniquely suited for this in the body. Specifically, it is able to non-invasively examine subcutaneous physiology in real time, capture signals in the vibration frequency range, and measure sub-microscopic displacements. Also important, it accomplishes these at a relatively low cost. The ultrasound method of choice, called (complex) quadrature phase demodulation, is a variant of Doppler ultrasound that was shown to measure tissue displacements in the 1980's\textsuperscript{20}. This method is in fact a modification of the phase locked loop method devised in the 1970's\textsuperscript{21}. When appropriately processed, quadrature phase demodulation can be used to measure the displacements associated with arterial vibrations, which can be as small as 30 nm.

The second issue in vibration detection and measurement is data analysis. Even with the myriad of modern signal processing techniques available, detection and measurement of transient oscillations with unknown onset, duration, frequency, bandwidth, amplitude and phase has remained elusive. This is true especially when the oscillation occurs in colored, non-stationary noise (i.e., frequency dependent and time varying noise) and in large, low frequency clutter, both of which are present in arterial vibrations.

We have developed a means to accomplish this detection and measurement based on the continuous wavelet transform. Use of the Morlet wavelet causes the transform to approximate a bank of matched filters for the vibration detection. The transformed data, then, are used for binary hypothesis testing for the presence of a signal in Gaussian distributed noise, as well as for estimation (measurement) of the vibration parameters. To evaluate the resulting detector, receiver operating characteristic (ROC) curves are generated using computer simulated vibrations.

2.1. Data capture with pulsed ultrasound

Data capture begins with pulsed ultrasound transmission and reception from a commercial diagnostic ultrasound instrument. The echo backscattered from each voxel of tissue is characterized by a particular amplitude and phase which are dependent on the character and position of the tissue. The received echo is thus both amplitude and phase modulated, which takes the mathematical form:

\[
S(\tau) = A(\tau) \sin(2\pi F\tau + \phi(\tau)),
\]

where \(S\) is a returned echo, \(A\) is the amplitude of the echo, \(F\) is the ultrasound transmission frequency, \(\phi\) is the phase of the ultrasound echo, and \(\tau\) is the time corresponding to the ultrasound propagation. The value of \(\tau\) is proportional to the depth, \(X\), of the tissue whose scatter produced the amplitude \(A(\tau)\) and phase \(\phi(\tau)\):

\[
\tau = 2 \frac{X}{c},
\]
where c is the speed of sound in tissue (~ 1.5 mm/µs) and the factor of 2 accounts for round trip travel of the ultrasound pulse. This expression dictates how a particular depth can be located based on the time elapsed between transmission and reception.

Equation (1) represents just one echo. For multiple transmit pulses, the received echoes will be time varying due to the time varying nature of the cardiac pulse:

\[ S(\tau, kT) = A(\tau, kT) \sin(2\pi F \tau + \phi(\tau, kT)) \]

where \( T \) is the time between transmit pulses and \( k \) is an integer representing the pulse number. For this discussion, variable \( \tau \) will be referred to as “fast” time with units of microseconds. The product \( kT \) will be used to represent “slow” time, corresponding to the phase or displacement changes at a given depth across multiple pulse echo cycles. “Slow” time is on the order of milliseconds or seconds. The received echo from a specific pulse-echo cycle (i.e., a fixed value of \( k \)) can be basebanded to yield:

\[ S_b(\tau) = A(\tau) e^{j\phi(\tau)} = I(\tau) + j Q(\tau) \]

Where \( j \) is equal to \( \sqrt{-1} \), and

\[ \phi(\tau) = \text{atan}(Q(\tau)/I(\tau)) \]

Note from equation (4), that \( I(\tau) \) and \( Q(\tau) \) will be 90° out of phase, which is a quarter of one period of the ultrasound. \( I(\tau) \) and \( Q(\tau) \) are therefore referred to as the quadrature representation of the received echo.

For a fixed value of \( \tau \), corresponding to a specific depth location from the ultrasound transducer, the phase of the returned echo, \( \phi(kT) \), is directly proportional to the displacement of the tissue that produced the backscatter according to:

\[ x(kT) = (\lambda/2) (\phi(kT) - \phi_0) / 2\pi \]

where \( \lambda \) is the wavelength of the ultrasound in tissue, \( \phi_0 \) is the phase of the returned echo at the initial pulse-echo cycle, the first factor of 2 accounts for round trip travel of the ultrasound pulse, and the second factor of 2 performs the unit conversion from wavelength to phase. By sampling the basebanded quadrature signals, \( I(\tau, kT) \) and \( Q(\tau, kT) \) in both “fast” time and “slow” time, displacements from multiple depth gates can be captured. This approach is similar to the methods used in Kanai et al.\(^{22} \) and Shinozuka and Yamakoshi\(^{23} \). It also has some resemblance to the methods of Hoeks et al.\(^{24} \).

For data collection, we use commercial diagnostic ultrasound instruments that have been modified to output a basebanded, quadrature representation of the received echoes. These quadrature data are either digitized directly within the instrument, or, for analog instruments, externally with synchronization to the transmission clock and pulse timing (400 MHz PC with a Gage Applied Sciences Compuscope 512 digitizer [Montreal, Quebec, Canada]). Offline analysis is carried out in MATLAB\(^{\text{®}} \).

2.2. Signal processing methods

2.2.1. Feature Extraction

Following data capture, the received data are parsed according to depth so that the detector and estimator can operate on data associated with a single depth at a time. Next, the data features need to be extracted to enable subsequent detection. Considering that a vibration is best distinguished from noise and clutter by its time and frequency characteristics, and that the vibrations of interest cannot be described in a compact mathematical model, the feature extraction method should be a non-parametric time-frequency transform, such as the Fourier transform or the wavelet transform.

Although the short-time Fourier transform (STFT) is applicable to transient data analysis, the time resolution at all frequencies is fixed by the arbitrary choice of the window length. An appropriate window length, though, is crucial to sensitive detection of the vibration. Since we know that the vibration can take on a wide range of unknown durations, the
STFT is not well suited for vibrometry. The STFT also is subject to high frequency bias when strong, low frequency clutter is present, further limiting its applicability for our purposes.

Alternatively, the wavelet transform has inherently fine time resolution at high frequencies and course time resolution at low frequencies, just as a short duration vibration would. The complex Morlet wavelet is particularly appropriate for vibrometry because the vibrations can be loosely considered sinusoidal and the quadrature values can be processed as complex numbers: $I(kT) + j Q(kT)$. In addition to its resemblance to a vibration (see Figure 2), this wavelet also provides superb clutter filtering as illustrated in Figure 3. Note from the figure that a vibration occurring at 130 Hz would pass unattenuated, while low frequency clutter occurring up to 75 Hz would be attenuated by more than 60 dB.

![Figure 2. Comparison of a vibration to a continuous sinusoid and a wavelet. The upper plot is the cluttered filtered vibration taken from one depth location in a stenosed human infrainguinal vein bypass graft.](image)

![Figure 3. Illustration of the clutter filtering ability of the Morlet wavelet with a quality factor of 3.](image)
2.2.2. Detection

For the same reasons that the wavelet transform is appropriate for feature extraction, it is also appropriate for vibration detection. The wavelet detector's primary role is in detecting signals that push conventional parametric and Fourier-based detectors beyond their capabilities. Specifically, they are most useful for detection when the expected signal is only roughly known, the noise variance is unknown, the noise is colored, the noise is non-stationary, or some subset of these. The wavelet-based detector is particularly useful in detecting non-stationary signals that in some way resemble the mother wavelet, such as in duration, bandwidth or shape. Wavelet detectors employ all wavelet types and many detection methods. A few wavelet detectors in the literature are relevant to arterial vibration detection. That is, these detectors apply when both the signal and the noise variance are unknown, as well as when the noise is colored. They use the one detection method that does not require a mathematical model of the signal: binary hypothesis testing for noise only. Two papers in particular address the use of the Morlet wavelet transform for detecting signals in Gaussian noise: Campbell\textsuperscript{25}, and Torrence and Compo\textsuperscript{26}. Although their methods apply only to stationary signals in either white noise or noise with a known spectrum, their technique forms the foundation for our vibrometry algorithm. Unlike Campbell, Torrence and Compo were determining confidence levels for signal analysis, not detection, but their results do apply to detection.

Both Campbell and Torrence and Compo make use of the fact that the wavelet power spectrum (the magnitude squared of the wavelet transform) of a Gaussian time series will be chi-square distributed with two degrees of freedom if either the data are complex, the wavelet is complex, or both. They proceed to outline a detection algorithm in which a signal is detected if ordinates of the wavelet power spectrum exceed the values expected of the chi-square distribution to a certain level of confidence. In other words, detection is made with the binary hypothesis test upon rejection of the null hypothesis that only Gaussian noise is present. Campbell's work required \textit{a priori} knowledge of the noise variance. Torrence and Compo's method accepted estimates of the noise variance, provided that the estimates were made from a long time series so that the statistics were not affected. Because the noise variance of arterial vibrations is not known \textit{a priori} and the noise variance is time varying, the noise estimates must be made on limited data lengths. We have, therefore, extended this detection approach to accommodate these adaptive noise estimates.

2.2.3 The novel detector

The role of the vibration detector is to estimate the noise level of the data and then to determine when a signal rises above the noise. To accomplish these, the Morlet wavelet transform is first applied to the raw quadrature data one depth at a time in order to condition the data by extracting the vibration features. The noise is then estimated from the transformed data. The detector further processes the data in order to use a statistical binary hypothesis test to decide the presence or absence of vibration. The test statistic used in the hypothesis test can be based on a time series from a single depth to determine the presence of a vibration. Alternatively, to exploit the \textit{a priori} knowledge that a vibration will have some spatial spread, the test statistic can be formed with time series from two neighboring depths. These steps are outlined below. Step 4b is optional; detection can be carried out with a time series from just one depth.

Step 1: Apply the wavelet transform to data from a single depth. The wavelet should be normalized for unit energy.
Step 2: Compute the wavelet power spectrum.
Step 3: Estimate the noise level adaptively using the minimum of two mean level detectors\textsuperscript{27} on the wavelet power spectral coefficients.
Step 4: Compute the ratio of each wavelet power spectral coefficient and its noise estimate, each divided by their equivalent degrees of freedom. The result will be called the "normalized wavelet power spectrum."
Step 4b: Repeat steps 1 through 4 for a neighboring depth and multiply the resulting ratio with the result of Step 4. The square root of this result will be called the "normalized cross wavelet spectrum."
Step 5: Detect vibration by rejecting the null hypothesis at a chosen level of confidence for the distribution expected from Gaussian noise. Reject detection hits that do not occur at both positive and negative wavelet center frequencies.

As exploited by Campbell, and Torrence and Compo, the results of step 2 are chi-squared distributed with two degrees of freedom. The deviation from their work arises with the noise estimate of step 3. For vibrometry, a noise estimate associated with a particular wavelet power spectral coefficient is computed from the minimum of the mean of two segments of wavelet coefficients at the same wavelet scale located symmetrically from the coefficient under test. The segments used for the noise computation must be located at least a full wavelet length from the coefficient under test in order to assure statistical independence. The two segments must also be separated by the maximum time duration expected for a vibration in order to ensure that at least one estimate is truly made from noise. Under the null hypothesis, the resulting noise estimate can be
shown to be chi-square distributed, with a multiplicative constant, to a very good approximation. The number of equivalent degrees of freedom, \( \nu \), of this chi-square distribution varies with wavelet scale, the specific wavelet used, and the length of the segment used in the estimation. The results of step 4, the ratio of two chi-square distributed variables, are F-distributed with 2 and \( \nu \) degrees of freedom under the null hypothesis. Step 4b makes use of the cross wavelet spectrum discussed by Torrence and Compo. It is the product of two identically distributed, F-distributed variables, again under the null hypothesis. For a complex Morlet wavelet with a quality factor of 3, and center frequencies ranging from 100 to 1000 Hz, the expected distributions match empirical distributions from Monte Carlo analysis out to confidence levels of \( 10^{-7} \). Details are given in Plett.

2.2.3 Estimation

Vibration parameters can be estimated from the wavelet coefficients. The vibration's duration is estimated simply as the time over which the vibration meets the detection threshold. Its frequency range is estimated from the frequencies spanned by the wavelet scales at which detection is made. Amplitude estimates must be made from wavelets normalized by the integral of their envelope. For example, the complex Morlet wavelet would be:

\[
w(t) = e^{-\alpha t^2/2} e^{j\omega_0 t} \sum_s e^{-\alpha t^2/2},
\]

where \( t \) represents discrete "slow" time, \( \alpha \) the taper decay factor, and \( \omega_0 \) the wavelet center frequency. In addition, the wavelet transform should be applied to the \( x(kT) \) time series of equation (6) for amplitude estimation (let \( t = kT \)); whereas, the quadrature time series can be used for the other parameter estimates. Instantaneous amplitude estimates are made from the sum of the wavelet coefficients across the scales at time and scale locations where the vibration meets the detection threshold. These estimates can be made arbitrarily accurate, after multiplication by a correction factor, by reducing the spacing between the wavelet scale center frequencies.

3. RESULTS

Monte Carlo simulation reveals excellent detection from both the single depth (step 4) and dual depth (step 4b) detectors. These achieve greater than 99.5% detection and 99.9% detection, respectively, for signal-to-noise ratios greater than or equal to 2 with less than 1% and 0.1% false alarm rates, respectively. The dual depth detector achieves greater than 99.5% and 98% detection rates with less than 1% false alarms at signal-to-noise ratios greater than or equal to 0.5 and 0.25, respectively.

The detection and estimation algorithms described here have been applied to in vivo data collected from various vibrations, including human stenoses, arterio-venous fistulas and pseudo-aneurysms with satisfactory results. Our results agree with the characteristics listed in Table 1. For ultrasonic arterial vibrometry, an additional list of descriptive parameters is important. These were acquired from our in vivo observations and are summarized in Table 2.

Table 2  Summary of additional vibration characteristics.

<table>
<thead>
<tr>
<th>Vibration characteristic</th>
<th>Minimum value</th>
<th>Maximum value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amplitude (nm)</td>
<td>30</td>
<td>4000</td>
</tr>
<tr>
<td>Signal to clutter ratio</td>
<td>0.001</td>
<td>1</td>
</tr>
<tr>
<td>Lowest signal frequency to highest clutter frequency ratio</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Signal to noise ratio (SNR)</td>
<td>&lt;1</td>
<td>&gt;10</td>
</tr>
</tbody>
</table>

4. SUMMARY

The vibrometry method outlined here uses pulsed ultrasound to capture potential vibrations. Quadrature signals demodulated from the received ultrasound echoes are parsed according to depth in tissue for subsequent processing. The detector operates on either the quadrature time series from a single depth or on quadrature time series from two neighboring depths.
estimator uses the phase of the quadrature time series to make displacement measurements. Both the detector and estimator are based on the use of the continuous wavelet transform as a filter bank with the complex Morlet wavelet used to approximate a matched filter for the transient vibration. A normalized wavelet power spectrum is used for detection in a single time series and a normalized cross wavelet spectrum is used for dual depth detection. Both of these detectors have excellent receiver operating characteristics as compiled from Monte Carlo simulation. These detectors have also been found to be effective on various vibration models, including examples of vibrations induced by true in vivo arterial disorders. The vibration amplitude, frequency and bandwidth estimates can be made arbitrarily accurate for data with large SNRs, with a tradeoff in computational cost. Duration estimation accuracy is affected by the choice of the wavelet duration.

In clinical applications, arterial vibrometry lends objectivity to the previously subjective, though routine, practice of auscultating bruits and murmurs with stethoscopes. Ultrasonic arterial vibrometry is potentially more sensitive than traditional auscultation, but this hypothesis requires validation. Certainly, though, vibrometry is significantly more resistant to environmental noise than the stethoscope method. Thus, the additional diagnostic information will not only contribute to improved diagnostic accuracy, but also: 1) enhance examinations in high noise environments, 2) assist in teaching, 3) permit examinations that are now impossible and, 4) aid the examiner with deteriorating hearing. When the algorithms described above are implemented in real-time, arterial vibrometry can begin to be used in clinical applications.

In the laboratory where arterial disorders are studied, the detector and estimator can make measurements that previously required invasive procedures. Not only will this allow measurements to be taken on animals without disturbing the experiment, but it will allow non-invasive measurements on human patients.

Finally, the arterial vibrometry detector and estimator described in this document provide a means of automatically detecting and quantitating oscillations with a thoroughness and sensitivity not previously available. While these methods have been designed specifically for arterial vibrometry, they apply to any situation in which the goal is to detect and/or estimate transient oscillations occurring in low frequency clutter and Gaussian noise. This Gaussian noise may be colored, non-stationary and with unknown variance.

ACKNOWLEDGEMENTS

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