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APPLICATION OF THE KHOKHLOV-ZABOLOTSKAYA-KUZNETSOV EQUATION TO MODELING HIGH-INTENSITY FOCUSED ULTRASOUND BEAMS

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APPLICATION OF THE KHOKHOLOV-ZABOLOTSKAYA-KUZNETSOV EQUATION TO MODELING HIGH-INTENSITY FOCUSED ULTRASOUND BEAMS

by

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ABSTRACT

High-intensity focused ultrasound is a form of therapeutic ultrasound which uses high amplitude acoustic waves to heat and ablate tissue. HIFU employs acoustic amplitudes that are high enough that nonlinear propagation effects are important in the evolution of the sound field. A common model for HIFU beams is the Khokhlov-Zabolotskaya-Kuznetsov (KZK) equation which accounts for nonlinearity, diffraction, and absorption. The KZK equation models diffraction using the parabolic or paraxial approximation. Many HIFU sources have an aperture diameter similar to the focal length and the paraxial approximation may not be appropriate. Here, results obtained using the “Texas code,” a time-domain numerical solution to the KZK equation, were used to assess when the KZK equation can be employed. In a linear water case comparison with the O’Neil solution, the KZK equation accurately predicts the pressure field in the focal region. The KZK equation was also compared to simulations of the exact fluid dynamics equations (no paraxial approximation). The exact equations were solved using the Fourier-continuation (FC) method to approximate derivatives in the equations. Results have been obtained for a focused HIFU source in tissue. For a low focusing gain transducer (focal length 50λ and radius 10λ), the KZK and FC models showed excellent agreement, however, as the source radius was increased to 30λ, discrepancies started to appear. Modeling was extended to the case of tissue with the appropriate power law using a relaxation model. The relaxation model resulted in a higher peak pressure and a shift in the location of the peak pressure, highlighting the importance of employing the correct attenuation model. Simulations from the code that were compared to experimental data in water showed good agreement through the focal plane.
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Chapter 1

What is HIFU?

High intensity focused ultrasound (HIFU) is a form of therapeutic ultrasound which uses high amplitude acoustic waves to heat and ablate selected tissue without damaging surrounding tissue. In addition to tumor necrosis, HIFU can also be used for hemostasis (stopping of bleeding) and immunotherapy[1]. It has been used in the treatment of prostate cancer, liver cancer, and uterine fibroids[2]. HIFU employs acoustic amplitudes that are high enough that nonlinear propagation effects are important in the evolution of the sound field. A common barrier to broad use is the determination of lesion location, where the lesion is the location of tissue destruction.

High intensity focused ultrasound has been in use since the early 1940’s by John G. Lynn and colleagues[3] at Columbia University. Lynn began with the use of HIFU in the propulsion of oil, melting of paraffin, beef liver changes, and radiation of the brain in dogs and cats by focused ultrasound. William and Francis Fry[4] at University of Illinois carried out research in the 1950’s that produced pinpoint lesions without damage to the surrounding tissue. Following this, they ablated parts of the basal ganglia in patients with Parkinson’s disease. At the same time in Russia, Burov et al.[1] found low intensity, unfocused ultrasound on cancer tumors had an increased immunological effect.

Focused ultrasound has been a treatment in a variety of cancers. Following in the work of Lynn et al. and Fry and Fry, HIFU has been used to necrose or cauterize tissue in the
brain, bone and soft tissue cancers, prostate cancer, pancreatic cancer, ocular melanoma, myocardial ischemia, and glaucoma[1]. More recently, in 2004, the FDA approved the use of HIFU in the treatment of uterine fibroids. Treatment of heart arrhythmias are currently undergoing FDA approval in the United States, and it is already used in Europe. In addition to tumor necrosis, HIFU can also stop bleeding in blood vessels in the case of emergency care, as well as fetal blood sharing.

There are several challenges to utilizing HIFU in a clinical setting. Transducers with large focusing gains are necessary to achieve the high intensity at the focus while keeping the surrounding tissue safe. However, despite use of large gains of the order of fifty, some patients end up with skin burning as a result of near field heating[1]. In addition, real time imaging of the area to be treated is needed to monitor the HIFU necroses. The presence of inhomogeneities in the tissue path means that the exact location of the HIFU lesion is hard to predict. Further, patients can move during the course of treatment, and this will affect the location of the lesion and the time needed for lesion formation. Ultrasound imaging of the lesions has yet to be reliable, and at present, MRI is used to monitor temperature in order to evaluate treatment. If an efficient tractable computer model could be developed to account for propagation into the body, then more accurate treatment could be performed. This should result in reduced risk of skin burning and potentially shorter treatment time.
Modeling of HIFU Beams

For a typical HIFU field, the peak pressure is approximately 10 MPa, the frequency is around 1 MHz, and the propagation distance is about 75 mm[1]. Modeling of HIFU beams therefore requires the incorporation of diffraction due to the use of a focused source, attenuation as the attenuation length scale in tissue is on the order of 100 mm at 1 MHz, and nonlinearity because the amplitude of the waves is high enough that small signal assumptions are violated. One measure of the importance of nonlinearity is to calculate the shock formation distance. For an initially sinusoidal plane wave, it is given by the expression

$$\bar{x} = \frac{\rho_0 c_0^2}{p_0 f_0^2 \pi^2 \beta}$$

where $\rho_0$ is the medium density, $c_0$ is the speed of sound, $p_0$ is the pressure amplitude, $f_0$ is the source frequency, and $\beta$ is the coefficient of nonlinearity. For typical HIFU parameters in water ($\rho_0 = 1000$ kg/m$^3$, $c_0 = 1500$ m/s, and $\beta = 3.5$), the shock formation distance is 140 mm at 1 MPa and 14 mm at 10 MPa. In practice, the wave is focused, so the pressure amplitude builds up and the shock formation distance cannot be simply expressed. However, for the range of pressures considered here, the distance is comparable to the propagation distance, therefore, nonlinearity is likely to be important.

The importance of nonlinearity in biomedical ultrasound has been demonstrated in both diagnostic and therapeutic ultrasound. Muir and Carstensen[5] first proposed that diagnostic ultrasound scanners might produce large enough pressures to cause nonlinear distortion as the pulse travels through the body. The initial interest in nonlinear effects was the
potential for enhanced heating caused by greater absorption of nonlinearly generated harmonics than the fundamental[6]. The first report of the observation of nonlinear distortion of imaging pulses in tissue was made by Starritt et al.[7]; both time domain and frequency domain effects were shown in their results.

Bacon et al.[8] compared two theoretical models for nonlinear propagation in medical ultrasound fields with experimental measurements from a 3.5 MHz focused transducer. One model used a full 3D finite difference method with a uniform transducer excitation function, referred to as the piston model. The other model utilized an approximation based on the beam profile with a Gaussian function. Bacon found that both models predicted the focal waveform for a high amplitude ultrasound beam to an accuracy of the order of 10%. The Gaussian model predicted the phase at high amplitudes less well, and it did not account for the near field diffraction of a real transducer. In addition, the piston model had to be closely matched to the experimental conditions, especially when the gain was low.

The role of nonlinearity in diagnostic ultrasound was reviewed by using the KZK equation to model circular, focused, and rectangular transducers in water, and extended to tissue-like media[9]. Several implications of nonlinear propagation were discussed. One implication is that nonlinear propagation generates harmonics, which makes the calibration of the ultrasound system more difficult. The higher harmonics are preferentially attenuated due to the increase in attenuation with frequency. As a result, there is a higher loss of energy from the beam, leading to enhanced heating. In addition, nonlinear propagation effects in water, like increased attenuation, do not occur as much in tissue. Although tissue attenuation can limit the generation of higher harmonics, nonlinear distortion in tissue is still significant. The generation of higher harmonics can be used in imaging, as the harmonics have narrower spatial width than the fundamental, and so lead to improved lateral resolution. Reduced side-lobe levels seen in the second harmonic make it easier to distinguish the true structures being imaged. The improved understanding of nonlinear propagation led to the conclusion that simpler and more efficient algorithms are necessary to predict nonlinear propagation, and tissue harmonic imaging, using the second harmonic to image,
is a continuing development.

Hynynen[10] conducted experiments quantifying the temperature elevation gains produced by high intensity focused ultrasound fields in a dog thigh in vivo. The results showed that for a single focused field, nonlinear propagation produced temperature gains as high as 2°C with continuous wave sonication elevating the temperature up by 5°C. It was concluded that nonlinear propagation could be used during HIFU, and temperature gains were high enough to justify further study.

Studies of hyperthermia in an in vivo canine model investigated the effect of nonlinear propagation when the ultrasound beam was scanned to heat a larger volume of tissue[11]. The results show that linear propagation should be used to determine which transducer to use, based on frequency and F number (F number = radius of curvature/transducer diameter). Although nonlinear propagation effects were not large enough to be a major design criteria, it does provide significant control over the power deposition and temperature distributions during the course of the treatment.

Moros et al.[12] compared theoretical and experimental ultrasound field distributions in in vivo dog muscle tissue, as well as in water. In general, good agreement was found between the simulated and measured pressure fields in water. Agreement could be improved if adjustments were taken to account for simulated versus measured focal lengths. In addition, the agreement was better in the focal region of the transducers rather than regions prior to the focus. It was argued that discrepancies were mostly caused by the nonideal behavior of the crystal, as the transducer may not have emitted energy uniformly over the surface. In muscle tissue, the main lobe in the focal region also agreed well between the theoretical and measured results. But the in vivo distributions showed side lobe enlargement, which is largely an indication of wave scattering. Because the enlargements were seen in the nonfocal plane distributions, this effect was not limited to the focal region. If the side lobe ultrasound field is not properly modeled, then treatment could be unsafe. Although this nonlinear model did well when compared to experimental data, the discrepancies are a strong motivation for using a fully three dimensional model.
Two numerical models for predicting temperature elevations were reported by Mahoney et al. [13] and results were compared to temperature elevations in in vivo rabbit experiments. One model assumed a source distribution from a uniformly radiating transducer, while the other used a source distribution by numerically projecting pressure field measurements from an area near the focus backward toward the transducer surface. Both models use the Rayleigh-Sommerfeld integral to calculate the pressure field. Using the pressure field as an input to the bioheat equation, the temperature in the tissue was calculated. The experimental data were obtained with transducers at 1.61 and 1.7 MHz combined with MRI, for temperature mapping. Temperature fields in water had excellent agreement between theoretical and measure fields. In tissue, the temperature fields were wider for the uniformly radiating transducer method than the backwards projection method. The results show that treatment planning was improved significantly by using the backward projection method in tandem with measured ultrasound field distributions.

Khokhlova et al. [14] have conducted experimental and theoretical work in the effects of nonlinearity, cavitation, and boiling on lesion formation in tissue phantoms. The research found that nonlinear effects were the main cause for accelerated heating until boiling occurred. Suppressing cavitation with overpressure (an elevated hydrostatic pressure used to dissolve bubbles) resulted in nonlinearity having a higher effect on lesion formation.

In the case where HIFU was necessary near the rib cage, Li et al. [15] discussed the effects of the ribs on the nonlinear sound field. Li developed a 3D numerical algorithm to solve the KZK equation in the frequency domain for the case of blockage by the ribs, and found good agreement between the experimental results and theoretical work. However, Bobkova et al. [16] have developed a method to minimize heating of the ribs while maintaining high focal intensity. Two methods were employed and tested with experimental data: one based on geometric acoustics and the other accounting for diffraction effects. The results showed that the diffraction method results in a better gain in focal intensity as well as less power loss on the ribs. The ribs typically cause a three way split of the focus, leading to a decrease in the focusing gain of the transducer. The experiments confirmed what the
models had shown, that the total power in the side foci are half of that of the main focus.

The first equation for diffractive nonlinear waves was the Westervelt equation[17], which made no restrictions on diffraction. This was followed by the KZK equation[18, 19] which employs a paraxial approximation for diffraction. Although not as accurate as the Westervelt equation, the KZK equation became popular as efficient numerical algorithms in both the frequency domain[20] and time domain[21] became available. Hajihasani et al.[22] developed a generalized time domain numerical algorithm to solve the diffraction term of the KZK equation. The technique was applied to the simulation of nonlinear propagation of ultrasound in tissue, using a five point IBFD (implicit backward finite difference) method to avoid oscillations in the near field. This technique solves the KZK equation in 3D Cartesian coordinates, allowing for a more accurate and efficient diffraction solution.

Christopher and Parker[23] developed a model for nonlinear diffractive field propagation which accounted for effects of refraction and reflection for propagation through multiple layers of fluid medium. They employed a Hankel transform technique to accurately model diffraction and attenuation under the assumption of one way propagation. Although their model could be applied towards ultrasound imaging, lithotripsy, and underwater sonar, their research ultimately compared water and in situ fields for ultrasound.

Ginter et al.[24] presented a nonlinear full-wave simulation model which, for a given transducer and initial pressure signal, predicted the generated ultrasound field. Using a second order approximation for the original hydrodynamic equations in ideal fluids that includes nonlinear steepening and formation and propagation of weak shocks, an explicit high-order finite-difference time-domain algorithm output the appropriate coefficients. Linear models underestimate the maximum pressure amplitudes not only at the focus, but also at the front of the wave. The experimental data was taken in water with a focused transducer of focal distance 55 mm. A 10% difference between the computational and experimental results was observed.

Following on from Ginter’s work, Liebler et al.[25] also conducted full-wave modeling for therapeutic ultrasound. In this case, a power-law attenuation model that captured the
attenuation of soft tissue was implemented in an efficient numerical time-domain method. Comparison between experiments in castor oil and simulations showed good agreement between the calculated and measured pressure time curves.

Recently, there has been much research in understanding how nonlinear effects can affect the meteorology of ultrasound fields. The differences in the absorption of water (where measurements are usually made) and soft tissue (where one wishes to estimate acoustic properties) can lead to dramatic changes in the evolution of nonlinear waves. A new derating method to extrapolate nonlinear ultrasound fields in water and tissue was reported by Bessonova et al.[26]. Their research showed that the discrepancy between derated focal peak pressures and modeled peak pressure in tissue was small for high focusing gains (40 in the linear scheme).

Matte et al.[27] have suggested a method for measuring pressure amplitudes using the KZK equation. By simulating the response of a circular single-element transducer in the far field using the parameters of the traducer and measurement position, the pressure measurements of the transducer could be made without using an extra transducer or hydrophone. This newer method of pressure amplitude measurement can lead to a more accurate model in high intensity focused ultrasound research.

More recently, Canney et al.[28] proposed a method to determine the HIFU field parameters at and around the focus which involved a combination of measurements and modeling. Nonlinear pressure waveforms were measured and modeled in both water and a tissue phantom for a 2 MHz transducer with an aperture and focal length of 4.4 cm. The input to a KZK-type numerical model was based on experimental low amplitude beam plots. Overall, the numerical simulations and experimental measurements were in good agreement. When steep shocks were present in the waveform for focal intensity levels higher than 6000 $\text{W/cm}^2$, lower values in peak positive pressure were observed for measured waveforms. These lower values were attributed to the broad but limited hydrophone bandwidth. Therefore, a combination of measurements and modeling enables an accurate depiction of HIFU fields.
Chapter 3

Models

3.1 Wave equation

The discussion begins with the classic equations of mass conservation, momentum, and state, taken as equations (1), (2), and (5) from Hamilton and Morfey[29]. The equation for conservation of mass can be written as

\[
\frac{D\rho^d}{Dt^d} + \rho^d \nabla \cdot \mathbf{u}^d = 0
\]  

(3.1)

where \(\rho^d\) is the mass density, \(\mathbf{u}^d\) is the fluid velocity vector, and \(\frac{D}{Dt^d} = \frac{\partial}{\partial t} + \mathbf{u}^d \cdot \nabla\) is the material time derivative. Here the superscript \(d\) is employed to denote a dimensional term.

The momentum equation can be written as

\[
\rho^d \frac{D\mathbf{u}^d}{Dt^d} + \nabla p^d = \mu \nabla^2 \mathbf{u}^d + (\mu_B + \frac{1}{3} \mu) \nabla (\nabla \cdot \mathbf{u}^d)
\]  

(3.2)

where \(p^d\) is the thermodynamic pressure, \(\mu\) is the shear viscosity, and \(\mu_B\) is the bulk viscosity. The generic form of the equation of state can be expressed as

\[
p^d = p^d(\rho^d, s^d)
\]  

(3.3)
If we express the field variables as perturbations to an ambient condition, that is, \( \rho^d = \rho_0 + \rho' \) where \( \rho_0 \) is ambient density and \( \rho' \) is the fluctuation in the density and \( p^d = p_A + p' \) where \( p_A \) is ambient pressure and \( p' \) is the fluctuation in the pressure. Here the \( ' \) terms are also dimensional, and the equation of state can be expressed as

\[
p' = c_0^2 \rho' + \frac{c_0^2}{\rho_0} \frac{B}{2A} (\rho')^2 + \frac{\kappa}{\rho_0} \left( \frac{1}{c_v} - \frac{1}{c_p} \right) \frac{\partial \rho'}{\partial t} \tag{3.4}
\]

where \( c_0 \) is the small signal sound speed, \( \kappa \) is the thermal conductivity, \( \frac{B}{A} \) is the parameter of nonlinearity for the medium, \( c_v \) is the specific heat at constant volume and \( c_p \) is the specific heat at constant pressure.

In linear acoustics, only linear terms are retained in these equations. In nonlinear acoustics, the so called “finite amplitude” approximation is involved, where second order terms are also retained. The assumption is made that \( |\rho'/\rho_0|, |u/c_0|, \) and \( |p'/\rho_0 c_0^2| \) are on the order of \( \epsilon \), a small ordering parameter. If terms of order \( \epsilon^3 \) and smaller are discarded, then the equations of mass conservation, momentum, and state, correct to second order, are (equations 30-32 [29])

\[
\frac{\partial (\rho')^d}{\partial t^d} + \nabla \cdot (\rho_0 + \rho') u^d = 0 \tag{3.5}
\]

\[
(\rho_0 + \rho') \frac{\partial u^d}{\partial t^d} + \nabla (p')^d + \frac{1}{2} \rho_0 \nabla (u^d)^2 = (\mu_B + \frac{4}{3} \mu) \Delta u^d \tag{3.6}
\]

\[
p^d = c_0^2 \rho^d + \frac{c_0^2}{\rho_0} \frac{B}{2A} (\rho')^2 - \kappa \left( \frac{1}{c_v} - \frac{1}{c_p} \right) \nabla \cdot u^d \tag{3.7}
\]

If the following dimensionless terms are introduced,

\[
\rho = \frac{\rho'}{\rho_0}, \quad u = \frac{u^d}{c_0}, \quad p = \frac{p'}{\rho_0 c_0^2}, \quad t = t^d f_0
\]
where \( f_0 \) is a characteristic frequency of the distance, e.g. frequency of the source, then the second order equations can be expressed as

\[
\frac{\partial \rho}{\partial t} + \nabla \cdot ((1 + \rho) \mathbf{u}) = 0
\]

\[
\frac{\partial \mathbf{u}}{\partial t} + \nabla \rho + \frac{1}{2} \left( \frac{B}{A} - 1 \right) \nabla \rho^2 + \frac{1}{2} \nabla u^2 = \eta \nabla \mathbf{u}
\]

\[
p = \rho + \frac{B}{2A} \rho^2 - \xi \nabla \cdot \mathbf{u}
\]

where \( \eta = \frac{f_0}{c_0^2} \delta \) with \( \delta \) as the diffusivity of sound, and \( \xi = \frac{f_0}{\rho_0 c_0} \left( \frac{1}{c_v} - \frac{1}{c_p} \right) \). This is the form of equations that will be solved using the Fourier-continuation technique.

### 3.2 KZK model

The KZK model begins with the dimensional form of the KZK equation, which stems from the paraxial approximation for diffraction[30].

\[
\frac{\partial p'}{\partial z^d} = \frac{c_0}{2} \int_{-\infty}^{t'} \nabla_\perp^2 p' \, dt'' + \frac{\delta}{2c_0^3} \frac{\partial^2 p'}{\partial (t')^2} + \frac{\beta}{2\rho_0 c_0^3} \frac{\partial (p')^2}{\partial t'}
\]

where \( p' \) is acoustic pressure, \( z^d \) is the propagation axis, \( \nabla_\perp^2 \) is the Laplacian in the lateral direction and for an axisymmetric source, \( \nabla_\perp^2 = \frac{\partial^2}{\partial r^2} + \frac{1}{r} \frac{\partial}{\partial r} \) where \( r \) is radial distance from axis, \( t' = t - \frac{z^d}{c_0} \) is the retarded time, \( \delta \) is the diffusivity of sound, and \( \beta \) is the coefficient of nonlinearity, which is defined as \( \beta = 1 + \frac{B}{2A} \).

The following nondimensionalization parameters were used to yield the nondimensional form of the KZK equation.

\[
\sigma = \frac{z^f}{z_f} \text{ where } z_f \text{ is the focal length}
\]

\[
\zeta = \frac{r^d}{a} \text{ where } r^d \text{ is the lateral distance and } a \text{ is the radius of the source
\[ \tau = \omega_0 t' \] where \( \omega_0 = 2\pi f_0 \) is the angular frequency and \( f_0 \) is the source frequency. 

\[ P = \frac{p'}{p_0} \] where \( p_0 \) is the source pressure.

Substitution of these parameters into the KZK equation yields

\[
\frac{\partial (P p_0)}{\partial (\sigma z_F)} = \frac{c_0}{2} \int_{-\infty}^{\tau'} \left( \frac{\partial^2 (P p_0)}{\partial (\xi a)^2} + \frac{1}{\xi a} \frac{\partial (P p_0)}{\partial (\xi a)} \right) dt' + \frac{\delta}{2c_0^3} \frac{\partial^2 (P p_0)}{\partial (\omega_0)^2} + \frac{\beta}{2 \rho_0 c_0^3} \frac{\partial (P p_0)^2}{\partial (\omega_0)}
\] (3.12)

which after rearranging some terms can be expressed as

\[
\frac{\partial P}{\partial \sigma} = \frac{z_F c_0}{2a^2 \omega_0} \int_{-\infty}^{\tau} \left( \frac{\partial^2 P}{\partial \xi^2} + \frac{1}{\xi} \frac{\partial P}{\partial \xi} \right) d\xi' + \frac{z_F \delta \omega_0^2}{2c_0^3} \frac{\partial^2 P}{\partial \tau^2} + \frac{z_F \beta p_0 \omega_0}{2 \rho_0 c_0^3} \frac{\partial P^2}{\partial \tau}
\] (3.13)

The following dimensionless parameters can be identified: \( A = \alpha_0 z_F \) is a measure of attenuation, where \( \alpha_0 = \frac{6 \omega_0^2}{z_0^2} \) is the attenuation at \( \omega_0 \), \( N = \frac{\overline{z}}{z} \) is a measure of nonlinearity, where \( \overline{z} = \frac{\rho_0 c_0^3}{p_0 \omega_0} \) is the plane wave shock formation distance at \( \omega_0 \), and \( G = \frac{z_0}{z_f} \) is the focusing gain at \( \omega_0 \), where \( z_0 = \frac{a^2 \omega_0}{2c_0} \) is the Rayleigh distance. The KZK equation can then be cast into the form that was used for calculations presented here.

\[
\frac{\partial P}{\partial \sigma} = \frac{1}{4G} \int_{-\infty}^{\tau} \left( \frac{\partial^2 P}{\partial \xi^2} + \frac{1}{\xi} \frac{\partial P}{\partial \xi} \right) d\xi' + \frac{A}{2} \frac{\partial^2 P}{\partial \tau^2} + \frac{N P \partial P}{2 \partial \tau}
\] (3.14)

Converting to \( x-z \) Cartesian coordinates, where \( x \) is the lateral distance and \( \xi = \frac{x}{a} \) yields

\[
\frac{\partial P}{\partial \sigma} = \frac{1}{4G} \int_{-\infty}^{\tau} \frac{\partial^2 P}{\partial \xi^2} d\xi' + \frac{A}{2} \frac{\partial^2 P}{\partial \tau^2} + NP \frac{\partial P}{\partial \tau}
\] (3.15)

### 3.2.1 Relaxation effects

For thermoviscous fluids, e.g. pure water, attenuation in the KZK equation is modeled by a frequency squared power law. However, for nonthermoviscous fluids like soft tissue, attenuation takes the form of a power law that is roughly linear in frequency[29]. Modeling this linear frequency dependency involves carrying out a convolution in the time domain,
which is a computationally expensive operation. In order to avoid this expense, we decided to approximate the power law with an attenuation law based on multiple relaxation frequencies.

In acoustic attenuation, relaxation processes are physical mechanisms in the equation of state that are governed by a rate equation with a single time scale. In the atmosphere and ocean, there are two primary relaxation processes. For the atmosphere, there is the vibration of nitrogen molecules and the vibration of oxygen molecules. In the ocean, there is the chemical dissociation of boric acid and magnesium sulfate[31]. For one relaxation process, the equation is given as

\[ \alpha_r(f) = \frac{B_r f^2}{f_r^2 + f^2} \]

where \( f_r \) is the frequency associated with the process and \( B_r \) is related to the amount of attenuation.

Here we choose to use two relaxation processes and a thermoviscous type attenuation to approximate tissue attenuation. In this case the attenuation can be expressed as

\[ \alpha_r(f) = \frac{B_{r_1} f_{r_1} f^2}{f_{r_1}^2 + f^2} + \frac{B_{r_2} f_{r_2} f^2}{f_{r_2}^2 + f^2} + B_{r_3} f^2 \]

(3.16)

where \( B_{r_n} \) are the relaxation coefficients, \( f_{r_n} \) are the relaxation frequencies, and \( f \) is the frequency.

For the tissue power law, the attenuation is given by

\[ \alpha_t(f) = \alpha_0 \left( \frac{f}{f_0} \right)^n \]

(3.17)

where \( \alpha_0 \) is the absorption coefficient at a characteristic frequency \( f_0 \), and \( n \) is the power law coefficient. For soft tissue, typical values are \( \alpha_0 = 2 \) Np/m at \( f_0 = 1 \) MHz and \( n = 1 \)[29].

To determine the appropriate parameters for the relaxation model, a mean square error between the tissue attenuation and the relaxation model in a frequency range of interest was used:
\[ \text{MSE} = \frac{1}{N_f} \sum_{i=1}^{N_f} |\log(\alpha_t(f_i)) - \log(\alpha_r(f_i))|^2 \]  \hspace{1cm} (3.18) 

where \( f_i \) are the \( N_f \) frequencies where the error was evaluated.

The MATLAB function `fminsearch` was used to determine \( B_{r1} \), \( B_{r2} \), \( B_{r3} \), \( f_{r1} \), and \( f_{r2} \). The routine required initial guesses for all five terms, and the default guesses used were:

\[ B_{r1} = 1 \times 10^{-6} \text{ Np/m/Hz} \]
\[ B_{r2} = 1 \times 10^{-6} \text{ Np/m/Hz} \]
\[ B_{r3} = 1 \times 10^{-16} \text{ Np/m/Hz}^2 \]
\[ f_{r1} = 2 \times 10^6 \text{ Hz} \]
\[ f_{r2} = 5 \times 10^6 \text{ Hz} \]

The frequency range was 300 kHz to 20 MHz in equally spaced log steps, resulting in \( N_f = 50 \). The optimization routine returned the following values: \( f_{r1} = 427917.987 \text{ Hz} \), \( f_{r2} = 4251966.499 \text{ Hz} \), \( B_{r1} = 3.482 \times 10^{-6} \text{ Np/m/Hz} \), \( B_{r2} = 2.834 \times 10^{-6} \text{ Np/m/Hz} \), and \( B_{r3} = 7.508 \times 10^{-14} \text{ Np/m/Hz}^2 \).

![Figure 3.1: Relaxation effects](image)

Figure 3.1 shows the plot for the frequency squared attenuation law, the power law for tissue which is linear in frequency, and the relaxation effects calculated using the parameters that minimized the error. Note that the curve for the relaxation effects model weaves...
around the tissue curve, as it does not have the exact power law but the optimization resulted in a good approximation of the power law. For comparison, a thermoviscous law \( f^2 \) that matches attenuation at 1 MHz is shown. It can be seen that the thermoviscous attenuation curves diverges away from the other curves at frequencies greater than 1 MHz. This is important for nonlinear propagation as the nonlinearity results in the production of harmonics and if the harmonics are not correctly attenuated, then there will be errors in the prediction of the acoustic field.

### 3.2.1.1 Variation of the initial guesses

To ensure that the minimization procedure was robust to the initial guess, the initial guesses were varied for each of the relaxation coefficients and relaxation frequencies. For these calculations, only one term was changed at a time, and the other terms were kept at the default initial values. In each of the tables, the changed value of the initial guess is shown, along with the percent differences in the calculated \( f_{r_1} \) and \( f_{r_2} \), and the mean square error at the end of the optimization.

<table>
<thead>
<tr>
<th>Initial ( f_{r_1} ) guess</th>
<th>Calculated ( f_{r_1} )</th>
<th>Calculated ( f_{r_2} )</th>
<th>Percent difference ( f_{r_1} )</th>
<th>Percent difference ( f_{r_2} )</th>
<th>MSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>( 4 \times 10^6 )</td>
<td>428031.726</td>
<td>4252975.957</td>
<td>0.02658</td>
<td>0.02374</td>
<td>0.054079</td>
</tr>
<tr>
<td>( 1 \times 10^6 )</td>
<td>427917.860</td>
<td>4251966.301</td>
<td>0.00003</td>
<td>0.000005</td>
<td>0.054079</td>
</tr>
<tr>
<td>( 0.5 \times 10^6 )</td>
<td>427917.906</td>
<td>4251966.777</td>
<td>0.00002</td>
<td>0.00001</td>
<td>0.054079</td>
</tr>
</tbody>
</table>

Table 3.1: Sensitivity of optimization algorithm to changes in \( f_{r_1} \)

In table 3.1, changing the initial \( f_{r_1} \) value to twice the initial value, half the initial value, and one fourth of the initial value resulted in negligible change in the final values of \( f_{r_1} \) and \( f_{r_2} \). The highest percent difference yielded was 0.02658%, for the case of \( 2 f_{r_1} \), which was considered acceptable. In addition, the mean square error remained 0.054079 for all three cases, suggesting that the search algorithm was finding the same minimum in each case.

Table 3.2 shows the impact of varying the second relaxation frequency by increasing to two times and three times the initial value. The highest value for percent difference
Tables 3.2-3.5 show the impact of halving and doubling $B_{r_1}$, $B_{r_2}$, and $B_{r_3}$. In all but one case, the changes to the optimized $f_{r_1}$ and $f_{r_2}$ are less than 0.00013%. The MSE also remains constant. The only notable difference occurred when $B_{r_2}$ was doubled. In this case, the differences in the optimized $f_{r_1}$ and $f_{r_2}$ were about 0.11% and the MSE
increased slightly to 0.054081. These differences were still considered small enough that the optimization algorithm was stable to changes in the initial guesses.

3.2.2 Source Conditions

Figure 3.2: HIFU setup for KZK model

Figure 3.2 shows a representative grid used for the simulations. The curved surface shows the physical source which was a spherical cap with a radius of curvature of 51 wavelengths. The radius of the source aperture was 10 wavelengths. The numerical grid was extended from the mouth of the source \((z = 0)\) to as far as output was desired; in these simulations the maximum distance was twice the focal length. In the lateral direction, it extended to three times the source radius.

The three parameters needed for the KZK equation are \(G\), \(N\), and \(A\). The source frequency was chosen to be 1.1 MHz for all the simulations. In this example, the medium properties were taken to be that of water, with density \(\rho_0 = 1000 \text{ kg/m}^3\), speed of sound \(c_0 = 1500 \text{ m/s}\) (resulting in a wavelength \(\lambda = 1.364 \text{ mm}\)), coefficient of nonlinearity \(\beta = 3.5\) (where \(\frac{B}{A} = 5\)), and diffusivity of sound \(\delta = 4.2745 \times 10^{-5} \text{ m}^2/\text{s}\). The focusing gain is
\[ G = \frac{\pi f_0 a^2}{c_0 z_F}, \] and for a geometrical focus of \( z_F = 50\lambda \), \( G = 6.28302 \). Focal length will be varied in other simulations. The attenuation \( A = \frac{\delta^2 \pi^2 f_0^2}{c_0^2} z_F \), and for this specific example, \( A = 0.020625 \). The nonlinearity parameter \( N = \frac{z_F p_0^2 2\pi f_0}{c_0^2 p_0} \), and for a source pressure \( p_0 = 1 \) MPa, yields \( N = 0.488679 \).

The source condition was taken to be a sinusoidal pulse of the form

\[
p = p_0 \sin(\tau) \exp\left(-\left(\tau / \pi n_{cycles}\right)^{2m_{env}}\right)
\]

(3.19)

where \( m_{env} \) is value of the exponent in the envelope function and \( n_{cycles} \) is the number of cycles in the envelope. For these simulations, the source frequency was taken to be \( f_0 = 1.1 \) MHz, and we chose \( n_{cycles} = 8 \) and \( m_{env} = 5 \). The resulting pulse is shown in figure 3.3. The curvature of the source cannot be directly incorporated into the KZK equation as it can only propagate fields from one plane to another. Therefore, the curved surface was migrated to the plane at the mouth of the source. The amplitude was kept constant but the focusing was affected by introducing a phase shift across the face of the source of the form \( \tau_s = \tau - Gp^2 \).

Figure 3.3: Pressure waveform for water case during parameter testing
3.2.3 Choice of Grid Parameters

For the test case shown in 3.2, the output of the KZK solution was checked for variations in the grid parameters. The performance was assessed by considering the peak positive pressure of the on axis waveform as a function of propagation distance. In these test cases, the simulations were carried out in the x-z Cartesian coordinates.

![Figure 3.4: A plot comparing the $\rho_{\text{max}}$ values for a single case](image)

The first parameter considered was the lateral size of the grid $\rho_{\text{max}}$. In figure 3.2, the parameter $\rho_{\text{max}}$ is equal to $\xi_{\text{max}}$. Figure 3.4 shows peak positive pressure as a function of axial distance for three different lateral grid dimensions, $\rho_{\text{max}} = 2$, $\rho_{\text{max}} = 3$, and $\rho_{\text{max}} = 4$. The differences between $\rho_{\text{max}} = 3$ and $\rho_{\text{max}} = 4$ were found to be less than 0.77%. At $\rho_{\text{max}} = 2$, two humps were observed at $\sigma \simeq 1.4$ and $\sigma \simeq 1.8$. These can be attributed to reflections from the lateral edge of the grid. For most of the simulations, a value of $\rho_{\text{max}} = 3$ was used. However, for a smaller source radius of $5\lambda$, a higher value of $\rho_{\text{max}}$ was necessary.
Figure 3.5: A comparison of the source parameter $\rho_{\text{max}}$ for the tissue case at source radius $5\lambda$. Left: Plot comparing the peak positive pressure for the three different $\rho_{\text{max}}$. Right: Zoom up of the plot to show irregularities at the end of the plot near $\sigma = 2$.

Figure 3.5 shows curves for a small source radius, $5\lambda$, where the differences between $\rho_{\text{max}} = 3$ and $\rho_{\text{max}} = 4$ was less than 0.8% until after the focus. After the focus, there are a series of irregularities in the form of bumps, which can be attributed to reflections from the edge of the grid. After zooming into the last irregularity, which is around $\sigma = 1.8$, the percent difference between the plots in $\rho_{\text{max}} = 3$ and $\rho_{\text{max}} = 4, 5$ at $\sigma = 1.75$ was less than 9.4%. It was therefore necessary to use $\rho_{\text{max}} = 5$ in calculations at a small source radius. Otherwise, $\rho_{\text{max}} = 3$ is sufficient for the calculations.

The next step in determining the grid parameters for the KZK solution was the number of points per piston, which determines how coarse the grid is in the lateral direction. Figure 3.6 shows peak positive pressure for the number of points per piston of 50, 100, and 200. Note that to see the differences, it was necessary to zoom in at the focus. The percent difference between 50 and 200 points was 3.56% and between 100 and 200 points was less than 2%. Because of this higher percent difference, the higher value of 200 points is used in the simulations. Increasing beyond this amount made the computational time excessive.
In the temporal domain, the parameter that was varied was the number of points per cycle. The value was varied between 500 and 2000 points per cycle, which corresponded to sampling rates of 550 MHz to 2.2 GHz. Note that this is much higher than the 1.1 MHz of the fundamental frequency but was necessary in order to capture the higher harmonics that are generated by the nonlinear distortion.

Figure 3.7 shows results as the number of \( \tau \) points per cycle was increased from 500 to 2000.
2000. Again, it was necessary to zoom in at the focus to see the differences, as seen in the right hand plot of figure 3.7. The percent difference between 500 points and 2000 points was 1.34%, therefore it was deemed that 500 points resulted in acceptable performance at reasonable computational cost.

To summarize, the equations of momentum, state, and conservation of mass correct to second order were presented. The KZK equation was presented, which assumed a sound beam (one way propagation) that satisfied the paraxial approximation. A time domain solution to the KZK equation was employed and appropriate grid parameters determined. It was found that using 500 points per cycle, 200 points per piston, and lateral grid distance of three times that of the source radius for the source parameters were sufficient for use in the calculation without making the computation time excessive. A method to determine the relaxation processes that fit the tissue attenuation curve was constructed, and in a comparison of the relaxation processes to thermoviscous effects, it was determined that the relaxation effects were found to be important enough to implement in the code.
Chapter 4

Results

Results for the numerical solution of the KZK equation will begin with a comparison of the predictions of the KZK equation in the linear regime with the O’Neil solution for a focused source. This will be followed by nonlinear simulations using the KZK equation for hyper-viscous water. The impact of using a more realistic tissue model will then be considered. Comparisons with experimental data are presented. Finally, comparisons between the KZK solution and the FC solution to the Navier-Stokes equations are shown.

4.1 Comparison with O’Neil solution

The O’Neil solution[32] is an analytical solution that predicts the axial pressure field for a focused source with a given wavenumber, k, radius of curvature, F, and radius of the aperture, a. For the comparison, we used the following parameters: radius of curvature $F = 69.53$ mm, radius of aperture $a = 13.64$ mm, and source frequency $f_0 = 1.1$ MHz. The medium was taken to be water with sound speed $c_0 = 1500$ m/s and density $\rho_0 = 1000$ kg/m$^3$. From these parameters, one can calculate wavenumber $k = 4.608 \times 10^3$ m$^{-1}$, Rayleigh distance $z_R = 0.4284$ m, and the focusing gain $G = 6.161$. The geometrical focal distance is $z_F = 68.18$ mm.

Since the comparison was between two linear cases, the water medium was used in
this simulation. The input parameters for KZK were $G = 6.28302$, $A = 0.020625$, $N = 0.488679$. However, because this is for the linear case, the nonlinear function in the code was turned off, and effectively, $N = 0$.

Figure 4.1: Plot of O’Neil solution with KZK model for linear water case

Figure 4.1 shows the peak pressure as a function of axial distance for the KZK and O’Neil solutions. In the vicinity of the focal peak, the solutions agree well. Note that the normalized peak amplitude is 7 and occurs at $\sigma = 0.8$, before the geometric focus and this is an expected result for a focused source. The first prefocal lobe is in reasonable agreement. Because KZK does not model diffraction accurately close to the source, the other prefocal lobes do not correspond with that of the O’Neil solution.

### 4.2 Hyperviscous Water Case

We now show how the presence of nonlinearity affects the field. For the water case, the medium parameters are as follows: density $\rho_0 = 1000$ kg/m$^3$, speed of sound $c_0 = 1500$ m/s, and coefficient of nonlinearity $\beta = 3.5$. The diffusivity should be $\delta = 4.2745 \times 10^{-6}$ m$^2$/s, however, this attenuation demanded very high temporal resolution for the waveforms,
at a high computational cost. To remedy this issue, the diffusivity of sound and by extension, the attenuation, was artificially increased by a factor of ten to $\delta = 4.2745 \times 10^{-5} \text{ m}^2/\text{s}$ and the medium is therefore referred to as hyperviscous water.

For a source pressure of $p_0 = 1 \text{ MPa}$, the input parameters into KZK are $G = 6.28302$, $A = 0.020625$, and $N = 0.488679$. Figure 4.2 shows peak positive pressure for the linear and nonlinear case. There are a series of lobes before the focus, which are all in agreement between the nonlinear and linear case before the focal peak, and is followed by the peak in the vicinity of the geometric focus at $\sigma = 1$. The effects of nonlinearity are very clear here, as the nonlinear simulation had a significantly higher normalized peak positive pressure of 17 and the focal point shifted from $\sigma = 0.8$ for the linear case to $\sigma = 0.85$ for the nonlinear case.
Figure 4.3: Waveforms at 20$\lambda$, 40$\lambda$, 50$\lambda$, and 80$\lambda$. Upper left: Pressure waveform at 20$\lambda$. Upper right: Pressure waveform at a point shortly before the focus, 40$\lambda$. Lower left: Pressure waveform at the focus. Lower right: Pressure waveform after the focus, at 80$\lambda$.

In figure 4.3, the pressure waveforms are shown for four locations along the axis. At 20$\lambda$, the behavior is close to sinusoidal, and the nonlinear and linear cases are in close agreement. Close to the focus, at 40$\lambda$, both waveforms have undergone distortion. There is steepening of the compressive part of the waveform in the nonlinear case, and the linear case is still symmetric. At 50$\lambda$, or the focus, the nonlinear waveform remains shocked and the peak positive pressure is close to 15 MPa, and the linear waveform remains symmetric. The nonlinear waveform is still shocked and asymmetric at 80$\lambda$ (30$\lambda$ beyond the focus), while the linear waveform is still symmetric.
Figure 4.4 shows a close-up view of the shock front for the position $\sigma = 0.5$. It can be seen that the rise time of the shock is very short and for the sampling rate employed here, there are 8 samples in the shock front. We note that this case was for hyperviscous water, and if the true viscosity had been employed, then the shock thickness would be ten times thinner and could not be modeled with the same sampling rate. A sampling rate of ten times higher would be needed to model water with usual viscosity.
Figure 4.5: Harmonics plot for hyperviscous water

Figure 4.5 shows the evolution of the harmonics along the axis for the nonlinear simulation. The fundamental frequency corresponds to the amplitude at 1.1 MHz. The second harmonic is the amplitude at twice the fundamental frequency, i.e. 2.2 MHz. At the source plane, all the harmonics have amplitudes less than 0.1% of the fundamental. As the wave propagates, the harmonics grow with distance. This is a hallmark of nonlinear propagation; the distortion observed in the time domain manifests itself in the frequency domain as the transfer of energy from the fundamental into the higher harmonics. Beyond the focus, the amplitude of the harmonics decays. The reduction in amplitude of the fundamental results in reduced nonlinear production of harmonics, and the diffraction and attenuation of the harmonics also reduces their amplitude.
Figure 4.6 depicts the spatial distribution of the harmonics (z vs. r) for hyperviscous water. For the fundamental and second harmonic, the prefocal peaks and nulls were evident. In the third and fourth harmonic, these prefocal peaks and nulls were less evident. It can be seen that all of the nonlinear harmonics are focused similar to the fundamental. However, the focusing is a little tighter in both the axial and lateral directions for the higher harmonics.

The effect of changing the source pressure was then considered. In this case, focusing gain and attenuation remain the same, at \( G = 6.28302 \) and \( A = 0.020625 \). At \( p_0 = 0.5 \) MPa, the nonlinearity parameter is \( N = 0.244340 \), half of the value for \( p_0 = 1 \) MPa. For
**Figure 4.7: Water case for various source pressures**

Figure 4.7 shows the peak pressure for the three source pressures. Beginning with $p_0 = 0.5$ MPa, the normalized peak pressure is 10 and occurs at a point close to the geometric focal point ($\sigma = 1$). At $p_0 = 1$ MPa, the peak pressure shifts back towards the source, and the normalized amplitude is higher than the 0.5 MPa case despite the fact that the pressure has been normalized by its source value. This means that doubling the source amplitude results in more than doubling of the focal pressure. With $p_0 = 2$ MPa, the normalized pressure peaks at 16, about double the value for 0.5 MPa, and the focus is shifted to prior to the focal point. These simulations illustrate the importance of properly modeling nonlinear propagation for the prediction of HIFU acoustic fields.

### 4.3 Tissue Case

For the tissue case, the medium parameters were as follows: density $\rho_0 = 1000$ kg/m$^3$, speed of sound $c_0 = 1540$ m/s, and coefficient of nonlinearity $\beta = 4.8$ (where $\frac{B}{A} = 7.6$). The attenuation for tissue was first approximated as a thermoviscous fluid with the diffusivity
chosen to match the attenuation at 1.1 MHz. A typical attenuation in tissue is 2 Np/m at 1.1 MHz, and this corresponds to a diffusivity of sound of $\delta = 6.4118 \times 10^{-4}$ m$^2$/s, which is 150 times the value for water. The source parameters were the same as in section 4.2 and using the parameters for tissue, yielded $G = 6.11982$, $A = 0.285882$, $N = 0.619311$. Note that A is much larger due to the higher attenuation and N is slightly higher as tissue is about 50% more nonlinear.

Figure 4.8: Tissue case for various source pressures

Figure 4.8 shows peak pressure for three different source amplitudes. Beginning with $p_0 = 0.5$ MPa, the normalized peak positive pressure hits at about 6.8 at $\sigma = 0.85$. At $p_0 = 1$ MPa, the peak positive pressure rises to 8.9 but does not shift and remains at around $\sigma = 0.85$. Even though the nonlinearity is higher, the extra attenuation reduces the amplitude of the wave, therefore decreasing the nonlinear effects which also attenuates the harmonics much more strongly. As the pressure is increased to $p_0 = 2$ MPa, the pressure rises further to 9.5 and the peak shifts towards the source with the peak occurring at $\sigma = 0.75$. 

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Figure 4.9: A comparison of the waveforms for various tissue pressures

Figure 4.9 shows a comparison of the focal waveforms at various source pressures for the tissue case. At 0.5 MPa, the waveform is close to sinusoidal, so there is little distortion resulting from nonlinearity effects. The waveform becomes slightly more distorted as the source pressure is increased to 1 MPa and 2 MPa, however, the effects are much less dramatic in comparison to the water case, figure 4.3. This is because the attenuation reduces the amplitude of the wave, resulting in a reduction of the nonlinear effects, which cause the distortions seen before in the water case.
Figure 4.10: Harmonics plot for tissue

Figure 4.10 shows the evolution of harmonics along the axis. In comparison to figure 4.6, it can be seen that the harmonics do not grow as much and this is why the waveforms are not as distorted. Note also the harmonics decay much more quickly beyond the focus due to the stronger attenuation, e.g. at $\sigma = 2$, the second harmonic had an amplitude of 0.3 MPa in tissue compared to 0.66 MPa for water.
Figure 4.11: Harmonics plots for tissue. Upper left: Fundamental harmonic. Upper right: Second harmonic. Lower left: Third harmonic. Lower right: Fourth harmonic.

Figure 4.11 depicts the spatial distribution (z vs. r) of the harmonics for tissue. For the fundamental, the prefocal peaks and nulls are clearly seen. The harmonics all show a similar focal spot close to the geometric focus. The distribution is similar to that predicted in water (figure 4.6). The axial extent is shorter due to the higher attenuation.
The effect that relaxation had on the simulation results is then considered. Figure 4.12 shows a comparison between the relaxation effects and thermoviscous effects for the linear tissue case. There is less than a 0.5% difference between the peak positive pressure for relaxation and thermoviscous attenuation laws, and the prefocal and post focal lobes show good agreement. This confirms that the two procedures attenuate the fundamental at the same rate.
Figure 4.13 shows the difference in the peak positive pressures for the relaxation and thermoviscous attenuation models for a nonlinear simulation with $p_0 = 1$ MPa. The prefocal lobes are in good agreement, indicating nonlinearity does not play a major role there. Close to the focus, the relaxation model predicts higher peak pressure with a peak value of 2.83 (about 10% higher than the linear simulation), and the location is shifted to $\sigma = 0.95$. This occurs because the relaxation attenuation does not attenuate the harmonic signals as quickly, allowing them to grow to larger amplitudes and result in higher pressures.

### 4.4 Comparison with experimental data

The experimental pressure field was created using a 1.1 MHz high intensity focused ultrasound transducer (Sonic Concepts H-101, Bothell, WA). The field was measured using a PVDF (polyvinylidene difluoride) membrane hydrophone (Precision Acoustics, UK). Similar to the sine wave propagated by the KZK equation, these field measurements also have a pulsed sine wave, which was provided by a function generator and amplified by a power amplifier (ENI A150 50 dB RF). The transducer had a 64 mm aperture diameter ($a = 33.1$ mm), and a focal length of $F = 63.3$ mm. Using the nominal source parameters in water, we calculate $G = 39.87526$, $A = 0.019148$, and $N = 0.020417$, where $p_0 = 0.045$ MPa was chosen to ensure the model matched the measured amplitudes.

Figure 4.14 shows the peak positive pressure as a function of axial distance. There was good agreement between the KZK model and the experimental data. The near field lobes and the main focal lobe are very well matched. Beyond the focus, the lobes do not line up quite as well. The KZK model is substantiated by experimental data, and thus further proving that the KZK equation is applicable to real life transducers.
4.5 Comparison with Fourier-continuation

The Caltech simulation utilizes Fourier-continuation (FC) methods to solve a spatial-spectral formulation of the second order Navier Stokes equations. Fourier transform based methods are better than finite difference methods at solving wave propagation problems over many wavelengths. Traditional Fourier transform based methods suffer from the Gibbs phenomenon if the boundary conditions are not periodic. However, the FC method takes a non-periodic problem and makes the data artificially periodic on a longer interval, reducing the Gibbs oscillations to an acceptable level[33].

The current implementation of the FC method is restricted to two dimensional Cartesian coordinates. The simulation reported here are therefore for two dimensional Cartesian coordinates. The focal length was held fixed at $50\lambda$, where $\lambda = 1.4$ mm and the source radius was varied between $5\lambda$ and $30\lambda$. The source pressure was kept at 1 MPa.
For the smallest source radius studied, $5\lambda$, the input parameters are $G = 1.52996$, $A = 0.285882$, and $N = 0.619311$. Figure 4.15 compares the peak positive pressure of the KZK and FC simulations. There is good agreement from $\sigma = 0.2$ through the end of the simulation. The only area where the solutions appear not to line up is very close to the source. However, this was to be expected as the KZK equation does not model diffraction close to the source very well.
Figure 4.16: Comparison of peak positive pressure for 10\(\lambda\) source radius

For a source radius of 10\(\lambda\), the input parameters are \(G = 6.11982\), \(A = 0.285882\), and \(N = 0.619311\). Figure 4.16 shows that the peak pressure through the focus still agrees well, although there is a 2% difference in amplitude. The first prefocal lobe also lines up moderately well, but the other prefocal lobes, that had previously matched up, no longer show good agreement. This suggests that as the aperture gets larger, the distance from the source where the KZK equation becomes valid increases. If one uses the metric that the parabolic approximation is valid for angles up to 20\(^\circ\), then for the 10\(\lambda\) source radius, the distance at which the KZK equation becomes valid is 27\(\lambda\) or \(\sigma = 0.55\). The data in figure 4.16 suggests this is a conservative estimate as agreement seems acceptable for distances as close as \(\sigma = 0.4\), which corresponds to an angle of about 26\(^\circ\).
The source parameters for a $20\lambda$ source radius are $G = 24.47929$, $A = 0.285882$, and $N = 0.619311$. The focal peak continues to match the FC solution, although there is now a 3.6% difference in the amplitude and also a difference in the distance at which the peak occurs, $\sigma = 1.006$ for KZK and $\sigma = 1$ for FC. Whereas previously, the first prefocal lobes agreed, now the first prefocal lobes no longer line up for this larger source radius. In addition, the other prefocal lobes do not agree with the FC solution. Using the $26^\circ$ criterion established previously for $10\lambda$, we would expect the parabolic approximation to be accurate at $\sigma = 0.5$, however, there are still discrepancies up to a distance of $\sigma = 0.8$. This suggests that there may not be a simple angle criteria for determining when the parabolic equation holds.

Figure 4.17: Comparison of peak positive pressure for $20\lambda$ source radius
At 30\(\lambda\) source radius, which is the upper limit of the size of HIFU sources, the dimensionless KZK parameters are \(G = 55.07840\), \(A = 0.285882\), and \(N = 0.619311\). Figure 4.18 compares the peak positive pressures and there are discrepancies throughout the domain and none of the lobes coincide. In particular, the peak pressure is predicted to occur at \(\sigma = 1.001\) by FC and at \(\sigma = 1.03\) by KZK. This difference corresponds to a shift of 2.03 mm in dimensional distance.
Figure 4.19: Comparison of the focal KZK and FC solutions at $20\lambda$ and $30\lambda$ source radii

Figure 4.19 is a comparison of the KZK and FC waveforms for the $20\lambda$ and $30\lambda$ source radii at the geometrical focus. Comparing the two solid lines, which are the solutions at $20\lambda$ source radius, there is still good agreement here, with the difference being 3.6%. For the $30\lambda$, the percent difference for the two solutions at source was 18.3%. Besides the large difference, the FC solution seems to be shocking and has shifted the curve to a time slightly before the KZK solution. This was also evident in the peak positive pressure plot, figure 4.18. These effects could also be attributed to the fact that the peak from the KZK simulation occurs after the FC, and so the nonlinear distortion for the KZK equation has not had a chance to affect distortion at this distance.
Chapter 5

Conclusions

The goal of this work was to define a parameter space where the KZK equation is valid with respect to sources employed for high intensity focused ultrasound, the motivation being to develop numerical tools that can predict the heating and tissue ablation in focused ultrasound surgery.

For a moderately focused source ($G \sim 6$), a robust simulation in water required using 500 points per cycle, 200 points per piston, and a lateral grid distance of three times that of the source radius in order for the calculation to complete without excessive computational time.

In the comparison of the linear water case with the O’Neil solution, it was found that the KZK equation accurately predicts the pressure field beyond $\sigma = 0.5$. This was consistent with expectations since the KZK equation does not model diffraction accurately close to the source. When nonlinearity was turned on, it caused shifts in the peak pressures and amplification of peak amplitudes. In water, the nonlinearity initially shifted the focus away from the source (i.e. defocused the beam), however at higher source pressure levels, the focus moved toward to the source. Amplification up to a normalized peak positive pressure of 17 was observed, compared to the peak pressure of 7 seen in the linear case (figure 4.2). In tissue, shifts were much less dramatic and the peak was translated back to $\sigma = 0.85$.

A method to determine the relaxation processes that fit the tissue attenuation curve
was constructed. A comparison of the predictions for a relaxation model and thermoviscous model of attenuation highlighted the importance of employing the correct attenuation model. The relaxation model resulted in a higher peak pressure (2.64 vs. 2.83) and shifted the location of the peak pressure from $\sigma = 0.88$ to $\sigma = 0.94$ which corresponded to a 4.2 mm shift in dimensional coordinates.

In a comparison with the Fourier-continuation method which solved the second order equations with no approximations, there was good agreement for smaller apertures, but as the aperture size increased, the discrepancies became noticeable. This was expected as the FC method captures diffraction exactly whereas the KZK equation uses a paraxial approximation. Agreement was reasonable for a gain $G = 25$, but for a gain of $G = 55$, the location of the focal peak shifted by a couple of millimeters. The Fourier-continuation method employed fewer points per wavelength (at 81 versus 500 for KZK). As such, the FC method has potential for faster calculations.

Comparison with experimental measurements for a HIFU source with $G = 39.87526$ showed good agreement through the focal plane. In conjunction with the comparison with the FC method, it appears that the KZK equation can predict acoustic fields to within about 5% for HIFU sources with gains up to around 50. This covers the range of many HIFU sources.

Future developments should address the incorporation of tissue inhomogeneities, a necessary step to take this research into the practical realm. This could be done within the axisymmetric paradigm only for layered tissues. To go beyond this would require a fully functional three dimensional model. It has been demonstrated that both nonlinearity and the appropriate attenuation law would need to be included in such a model. The KZK equation may be appropriate for this scenario as 3D versions have been developed[22] and it appears to be appropriate for focusing gains employed in HIFU. The next step in the model would be to incorporate a model to capture tissue heating and lesion formation. This would involve solving the bioheat equation (heat diffusion) and incorporating a model for tissue destruction.


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EDUCATION

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PRESENTATIONS
