COMPUTER SIMULATION OF FUNCTIONAL MATERIALS FOR THERAPEUTIC ULTRASOUND APPLICATION

by

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Abstract

"High intensity focused ultrasound treatment is a potential non-invasive treatment which uses ultrasound energy generated by a piezoelectric (ferroelectric) transducer to thermally ablate tumour tissues. However, the issue that is preventing the treatment from being more widely available is a prominent treatment cost in comparison to alternative therapies. The high treatment cost can be attributed to the longer operation time with cycles of heating and cooling. This heating and cooling cycle is applied in order to prevent overheating of the ferroelectric material which is used to generate the ultrasound. Overheating of the transducer can change the effective thickness frequency relationship of the material and can even lead to depolarization of the material. The overheating is caused by the energy loss (dielectric dissipation), which occurs when the alternating electric field is applied and converted into the ultrasound. The associated material characteristics are the quality factor or tan , which is a macroscopic property. Alternatively, the loss can also be related to the area of the hysteresis loop of the particular material. This project aims at searching for potential ferroelectric materials with reduced overheating which in turn means a material with reduced hysteresis area (or low tan). At the initial stage, first principle approaches have been adapted in our research rather than experimental methods, which would consume more effort in terms of equipment, capital and time. For the purpose of study, all electron density functional package WIEN2k with the help of high performance computing is being used. In order to determine the ferroelectric parameters which are related to the polarization based property of materials, an additional software BerryPI has been developed in the framework of our research. The property of interest (tan? or hysteresis

area) which is measured at macroscopic level has been brought down to microscopic level where it has been related to the barrier height of the potential curve of the ferroelectric materials. Based on this relation our plan is to perform screening of potential ferroelectric materials aiming at optimizing the produced mechanical energy to power loss ratio."

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Chapter 1

Introduction

1.1 Introduction to High Intensity Focused Ultrasound (HIFU)

When one thinks of tumor surgery the things that come to mind are an operative room, lots of instruments to incise the body with surgeons holding them and finally a long recovery time where the affected patient has to stay in special care for weeks, months or may be more. Such a treatment causes pre operative fear in patient's mind [10]. Such pre-operative fear can in turns results in long recovery time, negative emotions and in some cases it forces the patient to use analgesics [11]. These factors inspires people to develop an ideal tumor surgery which will avoid the above complications. An ideal tumor surgery would be a treatment which would require no incision and as a result shorter recovery time of the patient can be achieved This should be able to remove the affected tissue without damaging the adjacent structures near that tissue [9]. The non-invasive nature of the treatment would be able change

Figure 1.1: Focusing of ultrasound[1]

existing clinical practises and make it more patient friendly.

Magnetic resonance guided high intensity focused ultrasound treatment(MRgFUS) is considered to be a potential candidate for such an ideal tumor surgery [9]. In this treatment Magnetic resonance imaging (MRI) is used to localized the target tumor. Then an ultrasound energy is generated by vibrating a piezoelectric materials and focused on the target tumor tissue (Figure 1.1). The acoustic energy because of its unique nature just focused at the particular tumor tissue. Upon focusing the acoustic energy is converted into heat and thus thermally coagulate the tissue. The energy deposition doesn't cause any bio-effects to the adjacent healthy tissues or even tissues and skin on its path to the tumor tissue. The thermal ablation process require controlled monitoring in order to prevent overheating of tissues. MRI also has capability

[1] http://brainchemist.wordpress.com/2010/11/09/mri-guided-focused-ultrasound-surgery-radiology-brigham-and-womens-hospital-harvard

Figure 1.2: Compression and rarefaction of sound wave[2]

of mapping temporal and spatial distribution of tissues. This MRI feature is utilized to monitor the thermal ablation process..

1.2 Basic Principle

1.2.1 Ultrasound Generation

Ultrasound are basically sound waves with frequency greater than 1MHz. As human ear audible range is 20 Hz to 20000 KHz, it can't be heard by human being.Unlike other sound wave ultrasound propagate in a medium through vibration of molecules.First sound is generated from a source which initiate vibration. The vibration is transferred inside the medium to neighboring molecules. As a result compression and rarefaction takes place(Figure 1.2) where compression refers to the situation when molecules are pressed together or forced and rarefaction refers to the

[2]http://www.genesis.net.au/ ajs/projects/medical_physics/ultrasound/index.html

situation when the molecules are weakly bound or free to move.Moleculer vibration can take place in both longitudinal (longitudinal wave) and transverse(shear wave) direction. For medical ultrasound purposes shear wave is not used as it gets attenuated quickly is soft tissues [8, 1, 6, 7].

1.2.2 Ultrasound Transducer

Transducer is a device that converts one form of energy into another.Ultrasonic transducer is also one form of energy conversion device which converts electrical energy into mechanical energy using the piezoelectric effect.The transducer is operated at the resonance frequency of the piezoelectric material where it present higher response [12].The piezoelectric materials vibrates with the cycles of contraction and expansion in response to the electrical energy by means of alternating current. As a result compression wave and expansion wave is generated.Possible dampening of the sound wave might occurs in situation where during cycles of contraction and expansion, expansion wave generated is weakened by an expansion wave. This represents a situation where compression wave is generated in one side of the materials before the expansion wave from other side has left the material. In a similar way, compression wave can also be weakened by expansion wave to dampen crystal response. In order to avoid these situations careful control of the thickness of the piezoelectric materials according to the resonance frequency of the particular material. The established relationship between resonance frequency and the thickness is

$$t = \frac{n\lambda}{2} \tag{1.1}$$

Figure 1.3: Schematics of Ultrasound Transducer [3]

Here λ is the wavelength of applied frequency, n is an odd number and t is the effective thickness. If this relationship is maintained the compression or expansion wave when it reaches the end of the material is aided constructively by another compression or expansion wave and thus amplifies the ultrasound wave.

Figure 1.3 depicts a typical configuration of an ultrasound transducer. Its main component is the piezoelectric material which is mounted in a hollow metal or metal lined cylinder. Application of electric field to that material requires an electrical contact which is maintained by coating the faces of the crystal with thin conducting films. The front face of the piezoelectric material is coated protective plastic which ensure the efficient transfer of the ultrasound to the body. However as ultrasound is getting transferred through that plastic layer so its thickness is also important to prevent possible dampening of ultrasound due to cancelation of compression wave by tension or tension wave by compression wave. The effective thickness and resonance

[3] http://www.genesis.net.au/ ajs/projects/medical_physics/ultrasound/index.html

frequency relationship for the plastic coating is [5].

$$t_{plastic} = \frac{n\lambda}{4} \tag{1.2}$$

Here λ is the wavelength of applied frequency, n is an odd number and $t_{plastic}$ is the effective thickness of the plastic coating. The front face of the of the piezoelectric material is connected to aground potential and the remainder is insulted acoustically and electrically. As evident from Figure 1.3, on the back face of the piezoelectric there is a backing block which is hollow and contain just air. When an ultrasound wave is transmitted into the hollow cylinder it is reflected from the opposite end then reinforces the ultrasound that is moving in the forward direction to the body.

1.2.3 Piezoelectric Effect

The phenomenon of piezoelectricity was first discovered by Jcques and Pierre Curie in 1880 where the observed that under the influence of mechanical stress certain crystal undergoes electrification. [2]. Soon after that in 1881 a converse piezoelectric effect was derived mathematically by Lippman [4] using thermodynamic principles which was confirmed later by the curie brothers [3] on the same year. The latter effect was termed as indirect piezoelectric effect and the former one as direct piezoelectric effect. This phenomenon of piezoelectricity was observed only on certain materials like tourmaline,quartz,topaz,cane sugar and Rochelle salt mostly in the direction normal to polar axis. Based on this, it was concluded that this effect can be explained by the crystal symmetry study. Because of its unique nature, the discovery of piezoelectric materials created general interest among researchers which led this material find use in underwater sonar, medical imaging instrument, car accelerometers etc. In

Figure 1.4: The Piezoelectric effect

a piezoelectric material under equilibrium condition, the electronic charge distribution of the constituent elements are balanced equally between positive and negative charges in order to make the crystal electrically neutral. When perturbation is applied in the means of mechanical stress (Direct piezoelectric effect), the equilibrium charge distribution is compromised by the mechanical strain. The strain produces lattice mismatch as a result the charge distribution are arranged in a way to produce a net resultant electrification in the material. This charge distribution characteristics are expressed by polarization. Similarly in a indirect or converse piezoelectric effect when electrified, the charge distribution is arranged in accordance to the direction and characteristics of applied electric field. To accommodate this charge perturbation a net resultant strain is generated inside the material.

1.2.4 Ferroelectricity

Several crystal class exhibits piezoelectric effect but ferroelectric materials due to their singular behavior of switching between two equilibrium states have drawn significant

Figure 1.5: The ferroelectric hysteresis

attentions. Ferroelectricity was discovered in 1917 while investigating the piezoelectric properties of Rochelle salt. It was observed that these materials shows anomalous dielectric behaviors like the existence of a hysteresis between applied electric field and polarization, sudden change in piezoelectric behavior under certain temperature condition.

A ferroelectric material is described as an insulting system having equivalent but opposite multiple states of non zero polarization in the absence of any electric field. This non zero polarization is defined as the spontaneous polarization. These multiple spontaneous polarization states are switchable among each other by application of an external electric field.Another interesting property that ferroelectric materials posses is their ability to inherit several stable structural phases. In most common cases, their structural arrangement holds an ferroelectric phase below a characteristic temperature called the curie temperature T_c. At the ferroelectric phase the material contains lower number of symmetry operation with the absence of inversion symmetry and as a result, the net charge distribution produces a polar distortions of the structure to generate a non zero spontaneous polarization. But as soon as the material exhibit temperature higher than the curie temperature the structure undergoes a transformation from ferroelectric to paraelectric phase. At this structural phase a higher degree of symmetry is present inside the structure which balances out the charge distribution to maintain a zero spontaneous polarization.

It is obvious that the charge distribution disruption which generates the spontaneous polarization is produced by change in atomic arrangement of ions from their symmetric positions. So the crystal must be polar in order to exhibit a ferroelectric behavior. However, not all the polar crystal have the ability to switch their polarization between two equivalent and opposite state (or the ability to switch between two equivalent atomic position). So in order to be considered as a ferroelectric, the crystal must also demonstrate the switching behavior which appears in situation when there is a symmetry breaking distortion from the higher symmetry state. Figure 1.6(a) shows 2 dimensional view of perovskite crystal in polar phase. At this stage the distribution of atoms is highly symmetric which also give rise to a symmetric charge distribution. Thus the net resultant charge inside the crystal cancel each other to give structure with zero polarization. On the other hand, in Figure 1.6(b) the movement of atoms from their equilibrium position lowers the symmetry and the net charge distribution has a resultant in positive Z direction. The gives rise to a spontaneous polarization in that direction which confirms that the structure exists in a ferroelectric phase. Now, It is also evident from Figure 1.6(c) there is also an equivalent but opposite ferroelectric distortion is possible which gives to an equal spontaneous polarization in negative Z direction which represents the equivalent but opposite ferroelectric state.

Figure 1.6: Two dimensional ferroelectric distortion

1.3 Current challenge in High Intensity Focused Ultrasound

HIFU, despite of being one of the most promising treatment it is expensive. The majority of the high treatment cost comes from the involvement of MRI which costs about $4000 per hour for a typical HIFU treatment.Beside the treatment also involves charges for surgeon and other miscellaneous costs. A typical HIFU operation time time is very long(more than $2-3$ hours). which make a typical treatment cost of more than $10000 for a 2 hours treatment.Also during the whole operation,the patient are restricted to move which causes discomfort to the patient. MRI involvement during the treatment is essential as it monitors the thermal ablation process. But, the longer operation time which is responsible for the higher treatment cost comes because of a delay in sonication heating pulse. Figure 1.7 depict a typical heating and delay cycle applied during HIFU operation which suggests the time utilization efficiency of

Figure 1.7: Heating and delay cycle in HIFU treatment

around 30%. This longer delay in sonication is applied in order to prevent thermal build up due to cumulative build up of ultrasound near the transducer[Add reference]. This thermal build up if not prevented, can result in bubble because of boiling of water in the nearby tissue. Because of these bubble the focused ultrasound beam can get reflected or scattered near the bubble originating places places which in turn can results in deviation of path of the focused ultrasound.[Add reference]. Also from the transducer point of view, sufficient thermal build up can the expansion of the ferroelectric materials which will lead to the violation of effective thickness-resonance frequency relationship (Equation 1.2) and as a result dampening of ultrasound. And in worst case scenario, too much thermal build up can cause depolarization of the ferroelectric material if the temperature is near the curie temperature of the material. Besides during the sonication this thermal build up causes much discomfort to the patient.

Figure 1.8: Loss current in a dielectric

1.3.1 Factor to focus: Dielectric dissipation factor, Hysteresis

Thermal build up is resulted due to overheating of the ferroelectric materials during sonication and this is dependant on the ferroelectric material itself. The associated material characteristic is called dielectric dissipation factor, tanδ. Dielectric dissipation factor is a measure of parasitic loss that results by subjecting a material to alternating electric field. As shown in figure 1.8 when an electric field, E is applied in an ideal material the resultant charging current find itself out phase by 90^0 with the applied electric field. But in a typical ferroelectric material which is essentially a dielectric the current also has an loss component in phase with applied electric field and the net resultant current makes an angle δ with the ideal charging current. This loss current is a result of dissipation of energy as heat. This loss can interpreted using the parameter tanδ which is the ratio of loss current and charging current.

$$tan\delta = \frac{Loss\ Current, I"}{Charging\ Current, I'} \tag{1.3}$$

Now,the current flowing throw the material is related to the capacitance(C), applied electric field(E), frequency of the applied electric field(ω) and the dielectric constant of the material(ε) in the following way,

$$I = E\omega\varepsilon C \tag{1.4}$$

So the dielectric dissipation factor can also be express as a ratio of the complex part of the dielectric constant and real part of the dielectric constant.

$$tan\delta = \frac{\varepsilon"}{\varepsilon'} \tag{1.5}$$

The reason that there is a loss component is that during the application of alternating electric field to ferroelectric materials the polarization doesn't get enough time to attain equilibrium with the applied field. This lag is due to the fact that the forces in the system can't change according to the which it is subjected. Normally, in a process involve application of alternating current to a ferroelectric materials during ultrasound generation involves application of frequency in MHz range which means it gets time of around $1e^{-6}$ seconds. But as polarization requires much more time in order to attain equilibrium with applied electric field, this generates a lag between applied electric field and polarization.Mathematically, the applied alternating electric field has the following form,

$$E = E_0 e^{i\omega t} \tag{1.6}$$

Because of the lag in response the polarization has the following form,

$$P = P_0 e^{i\omega t-\delta} \tag{1.7}$$

Figure 1.9: Comparison of ideal switching and hysteresis loss

As a result of this delay, the polarization Vs electric field curve takes an hysteresis form(1.9).It is also apparent from Figure 1.9 that in ideal condition where is there is no lag in response of polarization with the applied electric field then the work done during the polarization switching would be the area under the rectangular curve. But as a result of failing to attend equilibrium, the work done during the polarization process is the area under the hysteresis curve. So the loss inside a ferroelectric material can be depicted by the shaded area shown in Figure 1.9. This consumed loss energy results in heating of the ferroelectric materials during a hysteresis cycle.

1.3.2 Research goal

There has been several studies on ferroelectric material to understand the phenomenon of overheating by thermal build up. But however, most of the studies were performed at a macroscopic level focusing mainly on growth conditions and mixture of various alloys with each other.But now a days as a result of tremendous development in high performance computing people are now focusing atomistic level simulation to understand those phenomenon at atomic level. Some atomistic level study has been performed just by considering forces acting on atom which didn't take the electronic interaction into account. There has also been some studies at atomistic level too to reveal the formation of domain wall in a ferroelectric materials.Also some studies has combined the ferroelectric parameters obtained from atomistic level simulation with macroscopic level phenomenon. But none of the studies focused understanding the phenomenon of switching at atomistic level using a model that includes all the possible important electronic interaction.

The goal of this research is selection suitable electronic structure method that include all the significant electronic interaction. Then using the method selected it will be necessary to establish a path to compute the relative ferroelectric parameters at the atomistic level.Once a complete method has been established then study of the underlying phenomenon of movement of atoms, growth of domains,suitability of switching during hysteresis cycle in a typical ferroelectric material. The findings from the study will assist in understanding the benefits of alloying in a particular ferroelectric which will eventually lead to design of a material will less thermal build up during sonication. Successful formation of such a material will reduce the treatment time during a typical HIFU operation and there by will reduce the cost of treatment. This will also insure better focusing of the ultrasound to the target by minimizing the risk of reflection and refraction. This will take HIFU an inch closer to being a patient friendly ideal tumor surgery.

Chapter 2

Figures and Tables

2.1 Figures

We can include encapsulated PostScript™ figures (`.eps`) in the document and refer to it using a label. For example, MUN's logo can be seen in Figure 2.1.

Figure 2.1: This is MUN's logo

Figure 2.2 shows a chart of MUN's Fall enrollment from 2005 – 2009.[1] The figure

[1] From *Memorial University of Newfoundland — Fact Book 2009.*

Figure 2.2: MUN Fall Enrollment 2005 – 2009

was created using the Calc spreadsheet application of the office suite OpenOffice.org.[2] This figure was reduced by 50%.

For larger figures, we can use landscape mode to rotate the page and display the figure using the `\munlepsfig` command, as shown in Figure 2.3. The figure will be the only thing on the page when typeset in landscape mode. (The figure is reduced to 85% of its original size.)

Alternatively, if we just want to rotate the figure, but not the entire page, we can specify an `angle` attribute in the default argument of the `\munepsfig` command. The result is shown in Figure 2.4. If the figure is too large or if there isn't sufficient text, then the figure may appear on its own page.

Note that all three of the enrollment figures are basically the same file, but with different names — on Linux, they are symbolic links to the same file. The filenames

[2] This office suite can be downloaded at no cost from `http://openoffice.org/`. Unlike other commercial office suites, OpenOffice.org may be legally shared with colleagues and fellow students. There are versions for Linux, Microsoft Windows, Mac OS X and Solaris. Also, unlike commercial offerings, OpenOffice.org does not require activation using registration keys.

Figure 2.4: MUN Fall Enrollment 2005 – 2009 (rotated)

have to be different because the reference labels need to be unique.

Figure 2.5 shows a Petri net created using the `xfig` program (`http://www.xfig.org/`) which has very good support for LaTeX. This figure has been reduced to 40% of its original size.

Figure 2.5: A deadlocked Petri net

We can also create figures of text (such as short code snippets) using the `\muntxtfig` command, as show in Figure 2.6.

```
#include <stdio.h>

int main(int argc, char **argv)
{
  printf("Hello world!\n");
  exit(0);
}
```

Figure 2.6: Hello World

2.2 Tables

We can also create tables, as seen by Table 2.1. Note that, as required by SGS guidelines, the caption for a table appears above the table whereas figure captions appear below the figures. Tables and figures can “float” — they may not appear on the page on which they are mentioned. LaTeX tries to handle figure and table placement intelligently, but if if you have a lot of them without a reasonable amount of surrounding textual content, the figures and tables can accumulate towards the end of the chapter. Generally speaking, if there is sufficient text explaining the tables and figures or if the tables/figures are relatively small, this may not be a problem. However, if you have a lot of tables or figures, it may be a good idea to put them in an appendix and refer to them as the need arises.

Table 2.2 shows a different table in landscape mode.[3] This is useful if your table

[3]This data was also taken from the *Memorial University of Newfoundland — Fact Book 2009*.

Table 2.1: Fall Semester Enrollment

	Undergraduate			Graduate		
	F/T	P/T	Total	F/T	P/T	Total
2004	13,191	2,223	15,414	1,308	879	2,187
2005	13,184	2,143	15,327	1,375	920	2,295
2006	12,809	2,224	15,033	1,373	899	2,272
2007	12,634	2,155	14,789	1,403	899	2,302
2008	12,269	2,208	14,477	1,410	1,005	2,415
2009	12,382	2,323	14,705	1,567	1,106	2,673

is too wide for the page. Tables are double-spaced by default. To single-space a table, change the `\baselinestretch` before beginning the table environment. Remember to restore it after the environment has ended.

Table 2.2: Masters Degrees Conferr

Degrees	2009 May	2009 Oct	2 May
Master of Applied Science	14	2	1
Master of Applied Social Psychology	1	5	
Master of Applied Statistics	0	0	
Master of Arts	37	49	2
Master of Business Administration	14	16	2
Master of Education	107	87	12
Master of Employment Relations	8	9	
Master of Engineering	20	19	2
Master of Environmental Science	3	3	
Master of Marine Studies	2	0	
Master of Music	4	1	
Master of Nursing	7	8	1
Master of Oil and Gas Studies	0	0	
Master of Philosophy	5	4	
Master of Physical Education	0	2	
Master of Public Health	0	8	

Chapter 3

Dealing with Errors

LaTeX can produce cryptic error messages at times. However, with some experience, it is usually not too difficult to determine what the problem is and how to fix it.

As mentioned earlier, appropriate search terms in Google may help you fix these error messages.

Chapter 4

Lorem Ipsum

Now, for your reading pleasure, some *Lorem ipsum*, courtesy of:

`<http://www.lipsum.com/>`

This gives a good view of the margins — note that the left margin is a bit wider than the right margin to accommodate binding.

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Chapter 5

Handling Citations

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Appendix A

Appendix title

This is Appendix A.

You can have additional appendices too (*e.g.*, `apdxb.tex`, `apdxc.tex`, *etc.*). If you don't need any appendices, delete the appendix related lines from `thesis.tex` and the file names from `Makefile`.