# BIOMEMS:
# THERMAL EFFECTS ANALYSIS OF DNA COCKTAIL SOLUTION (DCS) IN A MICROFLUIDIC CHANNEL

*(BIOMEMS: ANALISIS KESAN TERMA KE ATAS LARUTAN KOKTEL DNA DI DALAM ALUR BENDALIR MIKRO)*

By:
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67475

Supervisor:
ASSOCIATE PROFESSOR DR. ISHAK HJ. ABDUL AZID

March 2005

This thesis is presented to
Universiti Sains Malaysia
as a part of fulfilling the requirements for graduation with honours in
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## DECLARATION

This work has not previously been accepted in substance for any degree and is not being concurrently submitted in candidature for any degree

Signed……(candidate)
Date ……

STATEMENT 1

This thesis is the result of my own investigations, except where otherwise stated. Other sources are acknowledged by giving explicit references. Bibliography/references are appended.

Signed…….(candidate)
Date ……

STATEMENT 2

I hereby give consent for my thesis, if accepted, to be available for photocopying and for interlibrary loan, and for the title and summary to be made available to outside organizations.

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| | |
|---|---|
| **µMKSV** | Micro-Meter-Kilogram-Seconds-Voltage metric system |
| **Ag** | Argentum |
| **Ag-Pd** | Argentum-Palladium |
| **DCS** | DNA Cocktail Solution |
| **DNA** | Deoxyribonucleic Acid |
| **IC** | Integrated Circuit |
| **Ge** | Germanium |
| **LIGA** | *Lithographie Galvanoformung Abformung* (in German) |
| **LTCC** | Low Temperature Co-fired Ceramic |
| **max**. | maximum |
| **MEMS** | Microelectromechanical Systems |
| **min**. | minimum |
| **MKSV** | Meter-Kilogram-Seconds-Voltage metric system |
| **MST** | Microsystems Technology |
| **PCR** | Polymerase Chain Reaction |
| **Pd** | Palladium |
| **Taq** | *Thermus aquaticus* (in Latin) |

## ABSTRACT

BioMEMS and microfluidics technology are two areas of MEMS based application, which has found a lot of new grounds in the fields of medicine and health sciences. In a related development Polymerase Chain Reaction (PCR) is one of the areas where microfluidics MEMS can be applied. There are possibly a lot of new benefits such as reducing consumption of DNA cocktail solution (DCS), improving reliability, reducing the time it takes to complete the PCR process, using less power etc. A simulation of thermal analysis on static DCS in a single microfluidic channel under different conditions that includes environment and parametric changes are presented in this thesis. The analysis software ANSYS allows the creation of a simplified simulation model and also the thermal analysis of the model under the required conditions. The analyses include variation of heat generated from heater, change of ambient temperature and convection and also reduction of the heater size. All of which are analyzed under a no-flow condition environment with specific temperature ranges where the denaturing process and DCS is considered to be working optimally. The results are able to achieve the objectives and also to concur some of the theory presented from the literature. Besides that some new conclusive information on thermal effects due to parametric changes are also presented in this thesis.

# ABSTRAK

Teknologi BioMEMS dan mikrofludik merupakan dua bidang di dalam aplikasi MEMS yang telah bertapak kukuh di dalam industri perubatan dan sains kesihatan. Dalam satu perkembangan yang serupa *Polymerase Chain Reaction* (PCR) merupakan satu bidang di mana MEMS mikrofludik boleh diaplikasikan. Terdapat banyak faedah yang mungkin seperti mengurangkan penggunaan larutan koktel DNA (*DNA cocktail solution* atau DCS), meningkatkan reliabiliti, mengurangkan tempoh proses PCR, mengurangkan penggunaan tenaga dsb. Satu simulasi analisis haba ke atas DCS statik dalam alur mikrofludik tunggal di bawah keadaan-keadaan berbeza termasuklah perubahan persekitaran dan parameter dibentangkan dalam tesis ini. Penggunaan perisian analisis ANSYS membolehkan penghasilan model simulasi yang mudah dan analisis haba ke atas model tersebut di bawah keadaan-keadaan yang dikehendaki. Analisis-analisis dilakukan termasuklah haba dikeluarkan oleh pemanas, perubahan suhu sekeliling (*ambient*) dan perolakan (*convection*) sekeliling serta pengurangan saiz pemanas. Semuanya dianalisis di bawah keadaan persekitaran tak-alir dengan julat suhu yang spesifik di mana proses denaturasi dan DCS adalah dianggap berfungsi secara optimum. Keputusan yang dicapai dapat memenuhi objektif dan juga mampu mengesahkan beberapa teori yang diperolehi dari rujukan. Di samping itu, beberapa maklumat konklusif tentang kesan haba akibat perubahan parameter juga dikemukakan dalam tesis ini.

# CHAPTER 1: INTRODUCTION

In the USA, it is called *microelectromechanical systems* (MEMS) while Europeans call it *microsystems technology* (MST) (Elwenspoek and Wiegerink 2001). MEMS is also known by its community as the technology from *Lilliput* (Gad-el-Hek, Eds., 2002). *Lilliput* is a fictional land from the book *Gulliver's Travels* (Swift, 1726) where Gulliver meets a nation of people who are no bigger than his thumb. It is has been dubbed as the fourth technological wave where it is one of the most crucial developments in semiconductor technology (Tummala, Eds., 2001). Though it is known by different names, MEMS technology that plays a great role in providing actual physical contact with a designated operating environment.

## 1.1 Definition Of MEMS

Tummala Eds., (2001) defines MEMS as integrated microdevices combining electrical, mechanical, fluidic and optical components and also all physical domains, which range in size from micrometers to millimeters. Maluf, (2000) defines MEMS in broader terms that it is a technology having the objectives of miniaturizing complex systems by integrating a diverse set of functions into a small package.

## 1.2 Historical Background Of MEMS

On December 23rd, 1947, the transistor was invented, which initiated a fast-paced microelectronic technology revolution. In 1958, Jack Kilby built the first integrated circuit (IC) using germanium (Ge) devices that became first step in the development of miniaturization of systems. In 1965, Gordon Moore noted that chip capacities doubled each year, which became the famous Moore's Law. Hence, the complexity of IC's has doubled every two to three years with minimum dimension of devices is reduced to submicron levels. But control and measurement systems would be unable to sense without sensors to provide input from the surrounding environment and without actuators it won't be able to carry out the desired functions (Vittorio, 2001).

So attention was focused on developing microsensors and the first microsensor, which has been the most successful, was the silicon pressure sensor. In

1958, silicon strain gauges were developed commercially after it was discovered that the piezoresistive effect in Ge and Si had the sensitivity of 10 to 20 times greater than those based on metal films. Before 1987, micromachining techniques had been widely used to fabricate a variety of micromechanical structures. However these micromechanical structures were limited in motion to small deformations and were physically attached to the substrate. Elastic components were used as flexible joints, but their overall effectiveness in the design of mechanisms was limited. Mechanism can be employed for transmitting, controlling or constraining relative movement by a collection of rigid bodies connected together with joints (Vittorio, 2001).

It was only in 1987 to 1988 techniques for integrated fabrications of mechanisms on silicon were first demonstrated. It was now possible to fabricate mechanical parts such as gears, gear trains and linkages, which could complete unrestrained motion in at least one degree of freedom. This technology was the turning point that enabled the development of electrostatic micromotors and pushed the progress of other types of microactuators such as valves, pumps, switches, tweezers and lateral resonant devices. These advanced microactuators, which were comprised of a system of microdevices, are called *microelectromechanical systems* (MEMS). According to Vittorio (2001), the expression MEMS was first coined during a series of three workshops on *Microdynamics and MEMS* which were held in: -

a) July 1987 at Salt Lake City, Utah.
b) November 1987 at Hyannis, Massachusetts.
c) January 1988 at Princeton, New Jersey

## 1.3 Common MEMS Components

Most MEMS devices are designed and constructed to perform a single function. A clear trend in industries is to incorporate signal processing and closed loop feedback control systems into MEMS to make smarter integrated system. These systems are called the *lab-on-chip* concept where an entire unit can be contained in a silicon chip of a size less than $0.5mm^2$. In the past 20 years there has been relentless effort in developing and producing smaller and better MEMS device and components.

Using the LIGA (German acronym for *Lithographie Galvanoformung Abformung*) an advance micromolding process, it is possible to create a micromotor. This micromotor has all the components of an electrostatic driven motor that includes

rotor, stator and torque transmission gear. The toothed rotor has diameter of 700μm while the gear wheel has a diameter of 250μm diameter. The total height of the unit is only 120μm. Another important success was the creation of the microgear, which is smaller than an ant's head. This ceramic gear has a pitch of 100 micrometer is made using the LIGA technique. Besides that it is also possible to make microturbines (with rotor diameter of 130μm and total height of 150μm) capable of 150000 rpm with total lifetime of 100 million rotations. Though small in size it is capable of generating power similar to conventional turbines (Hsu, 2002).

## 1.4 Applications Of MEMS

Needless to say MEMS technology has found its way to many fields of science and engineering since its official coining in 1987. The major commercial markets for MEMS based products are industries that require high content of microsensors and microactuators. Automotive industry is the biggest player in the MEMS technology for the last 2 decades because of its market. MEMS make safer vehicles, a more comfortable drive, better fuel efficiency and less pollution. Major application of MEMS in an automobile can be divided into these 4 major areas, which are safety, engine, comfort and vehicle diagnostics (Hsu, 2002).

MEMS-based storage system is a secondary storage that provides higher density, lower latency and better power utilization compared with the current hard drives. This new storage technology based on MEMS is poised to fill a large portion of performance gap, significantly reduce system power consumption and enable many new applications (Gardner, et. al, 2001). The application of MEMS in aerospace systems offers new possibilities of increased capabilities, lower cost and lighter instrumentations. Helvajian and Janson (1999) outline a comprehensive application of MEMS in the aerospace industry.

## 1.5 Objectives And Scopes

Another emerging technology in MEMS is related in the field of biology. Hence the term BioMEMS, which is consequently the main subject matter of this thesis. One important biological process that applies this technology is called Polymerase Chain Reaction (PCR). The application of MEMS into PCR devices will reduce the use of DNA Cocktail Solution (DCS) and speed up the process greatly (Sadler, et. al., 2003). However the fundamental of thermal effects due to environment and parametric change for this device is not fully investigated. This project entitled *BioMEMS*: *Thermal Effects Analysis of DNA Cocktail Solution (DCS) In A Microfluidic Channel* will investigate one of the sub processes in the PCR technique. The major objectives and scope of this report will include: -

1. Conduct a simulated thermal analysis of static DCS in a single microfluidic channel under different conditions, which includes environment and parametric changes.
2. Understand the thermal effects on the DCS in the microfluidic channel under these different environment and parametric conditions.

Besides that the microelectronics involved will not be included in the scope of this thesis. In addition to that the scope is also limited to the denaturing step of the PCR process. Further information on the PCR process will be explained in *Chapter 2: Literature Review*. Although the concern of this thesis is the thermal effects to the DCS, it is however limited by monitoring the effects under certain temperature ranges. Under these temperature ranges the denaturing process is expected to work at an optimal level. Further information on these temperature ranges are disclosed in *Chapter 3: Analysis*.

# CHAPTER 2: LITERATURE REVIEW

The term BioMEMS describes the use of MEMS in biological based sensors and actuators. The biggest application of BioMEMS is in the field of biomedical and health sciences. BioMEMS is expected to revolutionize the way medicine is practiced and delivered. BioMEMS finds applications in the fields of microfluidics, drug delivery and transducers for surgical tools. This chapter will encompass some explanations on microfluidics MEMS, PCR and the BioMEMS technology that surrounds it before proceeding to the analyses in the next chapter.

## 2.1 Microfluidics MEMS And Biotechnology

Microfluidics is a MEMS technology that addresses the miniaturization of composite devices and systems and the study of application associated with the handling of liquids and gases (Zhang et.al., 2002). MEMS in relation to microfluidics requires the ingenuity of creating devices and processes that deal with volumes of fluid on the order of nano liters ($10^{-9}$ liter) or pico liters ($10^{-12}$ liter) (Maluf, 2000). A MEMS device of this class is able to perform environmental sensing, control actuation, biomedical analysis, agent detection and precision fluid dispensing.

It offers the advantages in terms of improved parameter control, reduced power dissipation, increased system reliability, size reduction, minimal invasive surgery procedures, more precision, reduced reagents consumption, real-time processing and reduced manufacturing costs. It has commercialized some of its application into the consumer market. According to System Planning Corporation Market Survey, microfluidics MEMS devices have the largest sales volume for all MEMS based equipment. In 1996 it has sales between 400 – 500 million Euros and 3000 – 4450 million Euros in 2000 (Gardner, et. al, 2001). Two of its prominent application includes the manifold absolute pressure sensor in the automotive sector and the inkjet printer head (Elwenspoek and Wiegerink, 2001).

The past two decades, researches have worked on a number of microfluidics MEMS applications including microvalves, pumps, filters, mixers, cooling systems etc. However biggest future market for the microfluidics MEMS technology is biomedical and health sciences. So biomedical and pharmaceutical industries have

supplied the primary motivation for the rapid development of microfluidic technology in the BioMEMS field (Micronit, 2004), (Roche, 2003), (Eppendorf, 2005), (Brinkmann, 2004). Some of these include miniaturized chemical and bio-analytical tools, lab-on-chip systems, diagnostics microchips, miniaturized bioassays, DNA amplifiers etc. Consequently, PCR techniques using microfluidics MEMS are also part of this growing technology (Figure 2.1).

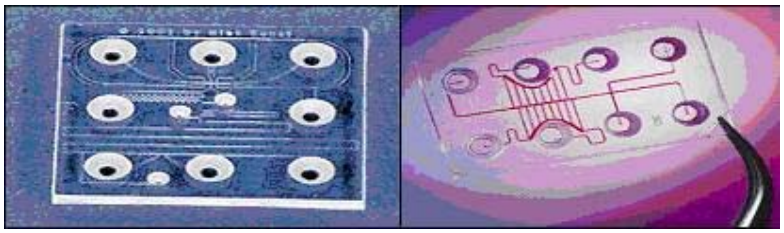


Figure 2.1: Two lab-on-chip devices with microfluidic channels etched on them. *[Note: Both chips are capable of doing what usually requires days of lab work within matters of hours to minutes (Weigl, 2000), (Micronit, 2004).]*

## 2.2 Polymerase Chain Reaction (PCR)

All genetic code of every living organism is stored in chromosomes, which contain long chains of deoxyribonucleic acid (DNA). The objective of genetic diagnostics is to decipher the sequence of nucleotides in a DNA fragment after its extraction and purification from a nucleus cell. But the task is difficult due to the tiny concentration of DNA available from a single cell. This was even harder when it involved limited, rare, fragile and old DNA samples [Powledge, 2004].

But all this changed in 1983 when Kary Mullis conceived the PCR method, which won him the 1993 Nobel Prize in Chemistry. The PCR is an enzymatic method of synthesizing large quantities of a targeted region of DNA in-vitro from a single DNA fragment. The basic idea is to physically separate two strands of double helix DNA cell, then use each strand as a template to create a complementary replica (Roche, 2003). Potentially it is possible to generate millions of copies of a specific segment of DNA even from a single initial copy (Vierstraete, 1999). The PCR method is so indispensable in molecular biology that it is difficult to do without it. Because of

the PCR method insufficient DNA problem is no longer a limitation in molecular biology, medical diagnostic, bio-anthropology and archeology (where limited, fragile DNA samples of animals or people can be thousand to millions years old and in very poor condition). Even forensics and criminal investigation apply PCR for DNA fingerprinting. More importantly, researchers have continually updated the definition of PCR applications by increasing the usefulness and scope of the technique (Powledge, 2004).

## 2.3 Denaturation

The three major processes in PCR are denaturation, annealing and extension. But for the purpose of this thesis only the denaturation process will be explained. It is noted here that the DNA cocktail solution (DCS) contains the DNA sample or template, enzyme and other additional contents, which are vital for the overall PCR process. More information on the entire PCR method can be found from Biotech Adventures, (2004), Roche (2003), Vierstraete, (1999), Brinkmann (2004) and Eppendorf, (2005).

During a denaturation step (in a standard PCR process) the DCS, which contains the DNA sample, is exposed to high temperature of 90$^{o}$C – 96$^{o}$C (Brinkmann, 2004), (Powledge, 2004). This temperature will denature the DNA, creating two complementary single strands of DNA, which is exposed at the nucleotide bases (Figure 2.2). The high temperature in the denaturing step has the advantage of separating proteins and disrupting cells so it is not required to start with a purified DNA template. This allows for even a poor quality DNA template to be used (Powledge, 2004). However it is also possible that excessive high temperature may cause DCS to overheat and damage its contents whereas a temperature too low may cause denaturing process unable to work at an optimal level or becomes completely inactive.

PCR is an enzymatic approach, which means it requires an enzyme to work. A standard PCR process requires Taq polymerase or enzyme, which is introduced into the DCS prior to the denaturing step. Taq is a thermo-stable polymerase isolated from the *Thermus aquaticus* bacteria, which is originally from hot springs in Yellowstone National Park, USA. However, if the temperature is too high the Taq enzyme will begin to breakdown and will not be able to perform the extension process later. Hence more enzymes will be required. So it is usually at this denaturation step where the

enzyme easily breakdown. Hence it is vital at this denaturation stage that the DCS is always within the recommended temperature range. All this requires constant monitoring and regulating. This is where MEMS technology comes in.

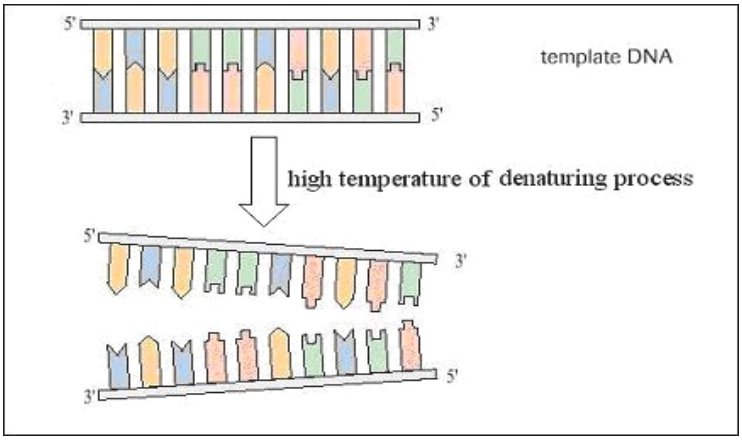



Figure 2.2: Denaturation creates two complementary single strands DNA from the template DNA (Adapted from Brinkmann, 2004).

## 2.4 MEMS And PCR

Integrating MEMS into PCR can have a wide range of benefits. This is possible by using a lab on chip device concept. A PCR device using MEMS technology will be able to reduce the use of DCS, better control of parameter, use less power, increased process reliability, size reduction, increased precision, real-time processing and reduced manufacturing costs. All these factors are important since PCR deals with miniscule elements, which can easily be contaminated and damaged. Hence another important factor in PCR is thermal control. Since a PCR device using MEMS technology is relatively small, it is easily affected by environment conditions or parameter change. Furthermore, the denaturing process needs to be in the correct temperature range for it to be at an optimal level. Consequently, all these factors are elements of this thesis that will be investigated.

## 2.5 Current Research On MEMS Based PCR Devices

Although there is a number of MEMS based PCR devices available in the market, not much literature on thermal effects analysis can be found. There is much information on what the thermal situation in PCR should be but no analyses are thoroughly investigated. Sadler et. al. (2003) has completed an analyses on a PCR device using simulation and experimental procedures. While the experimental effort looks promising but still the work lacks in terms of thermal effects analysis and its fundamentals. The simulation is mostly used as a prerequisite in building the experimental model.

So this provides an opportunity to return back to the basics where fundamental thermal effects analysis in a simulated environment can be conducted. Changing of parameter and environment conditions allow more in depth understanding of the basics thermal elements of MEMS based PCR devices.

# CHAPTER 3: ANALYSIS

As previously noted, Sadler, et. al. (2003) conducted a simulation and experiment on a MEMS based PCR device. The simulation model was performed using CFDRC ACE+. This software is well suited for conducting thermal-microfluidic-BioMEMS based simulation and analysis (CFDRC, 2004). However for the purpose of this thesis (and the available facility at the Mechanic School), the software ANSYS 8 was used instead. ANSYS 8 is able to conduct analysis for structural-MEMS reasonably well but has some limitation for solving thermal-microfluidic-BioMEMS based analysis.

The analysis will only involve the channel used in denaturing process of the PCR technique. The denaturing process was selected because it requires the highest amount of heat hence a lot of the thermal effects can be observed here. So to accommodate for this reason the PCR device model (Sadler, et. al., 2003) is modified.

## 3.1 Assumptions

Some vital assumptions were needed to conduct the simulation and analysis for this thesis. Assumptions are required since they also provide some boundary conditions for the analysis. These assumptions include: -

1) The fluid in the channel is considered motionless (static or no-flow condition).
2) In the absence of any bulk fluid motion, heat transfer between a solid surface and the adjacent fluid is by pure conduction (Cengel, 1997). This is a fundamental heat transfer theory, which is applied in the entire analyses. This theory is important in explaining why heat transfer through convection is not included for the heat transferred from the internal integrated heater-to-ceramic base-to-DCS in the channel. As an added information, Cengel (1997) gives convection by the equation of heat transfer rate in natural convection from a solid surface to the surrounding fluid is expressed by Newton's law of cooling as: -

$$Q_{conv.} = hA\,(T_s - T_\infty)$$

Equation 3.1: Newton's law of cooling by natural convection.

Where: -

$Q_{conv}$ is heat transfer by convection (W).

h is the average heat transfer coefficient by convection ($W/m^2K$).

A is the heat transfer surface area ($m^2$).

$T_s$ is the surface temperature (K).

$T_\infty$ is the temperature of fluid far from the surface (K).

3) In a no-flow condition, where heat transfer only occurs through conduction, the temperature within the channel and the entire ceramic base will be higher. Further explanation on this assumption will be provided later in this chapter. As an added information here, Cengel (1997) gives conduction by the equation of Fourier's law of heat of conduction as:

$$Q_{cond.} = -kA\frac{dT}{dx}$$

Equation 3.2: Fourier's law of heat conduction.

Where: -

$Q_{cond.}$ is heat transfer by conduction (W).

k is thermal conductivity of the material (W/mK).

$dT$ is the difference of temperature between two points or planes (K).

$dx$ is the thickness or distance between two points or planes (m).

4) Optimal temperature range for the DCS and denaturing process is between 90°C to 96°C (Powledge, 2004). But Sadler, et. al. (2003) gives a range of 93°C to 95°C since it was required a ± 1°C from the optimal temperature of 94°C. However this fact can be debated on grounds that many products available in the market allows a different range of temperatures (Brinkmann, 2004), (Eppendorf, 2005), (Micronit, 2004). Some are low as 85°C while others as high as 99°C. This is dependent on the fact that some DCS may use different variants of enzymes/ chemical solution. Plus some fragile DNA samples (which are decades to centuries old) require a much lower temperature since there is a high possibility of damaging the rare sample (Brinkmann, 2004). Besides that Sadler, et. al. (2003) also shows that the simulation's highest temperature is 97°C. On an analysis level consideration, the temperature range of 90°C to 96°C allows better observation of temperature contours. So to not further complicate matters, temperature range

of 90°C – 96°C will be the main observation. While the 93°C – 95°C temperature range is observed as a further additional analysis or as a tighter control of the latter.

5) Although convection does not occur between DCS and the surface of the channel's internal walls, it does however occur on the outside surface of the ceramic base. The importance of this external convection and also the ambient temperature is explained later. It is noted here that the ambient temperature that surrounds the external surface of the ceramic base is set at 20°C while the convection on the external surface of the ceramic base is set at 20W/m$^2$K.
6) The temperature of the DCS at the channel entry is set at 40°C, which is the incubation temperature of DCS prior to the denaturing process (Eppendorf, 2005) and (Brinkmann, 2004). The actual range is between 35°C to 45°C so average of 40°C is taken.

## 3.2 Model Description

Sadler, et. al. (2003) provided the original model with the size of 20mm (length) x 19mm (width) x 2.4mm (thick). This is the size of three-channel model, which is able to complete the entire PCR process (Figure 3.1). However for the purpose of this thesis, the original model has been modified to accommodate for a single channel in a no-flow condition analysis. Modification includes model length is reduced to 4mm (Figure 3.2). This leaves with a new dimension of 4mm (width) x 19mm (length) x 2.4mm (thick). A quick note here is that the new length was previously the width and the new width was previously the length.

This modified version is without the air gaps. Air gaps based on the original model provide thermal isolation. This means it creates a thermal barrier/ shield to avoid the heat to be transferred from one channel to another. This feature is not required since the analysis performed will be concentrating on the thermal effects within the channel boundaries only. As for the channel's dimension it is set at 0.5mm x 0.5mm x 19mm (length) (Sadler, et. al., 2003). Note the channel length is adjusted so the channel goes through the ceramic base. The single channel is given an entry and exit to provide a sense of direction for the static DCS (DNA cocktail solution).

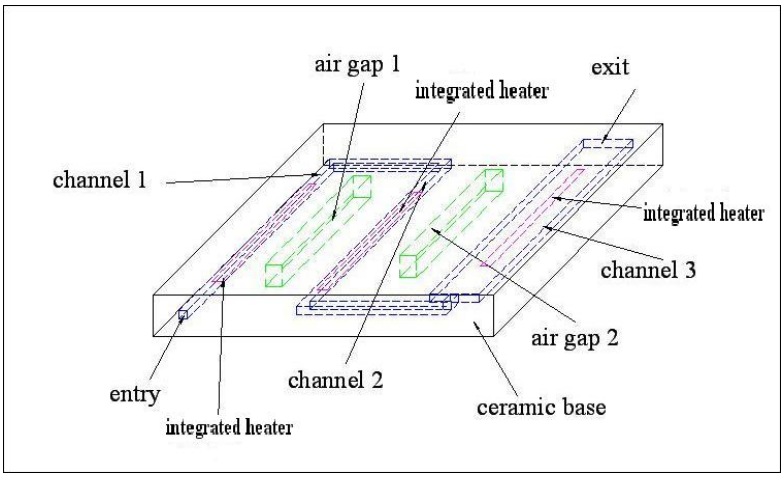



Figure 3.1: The original 3-channel model PCR device.

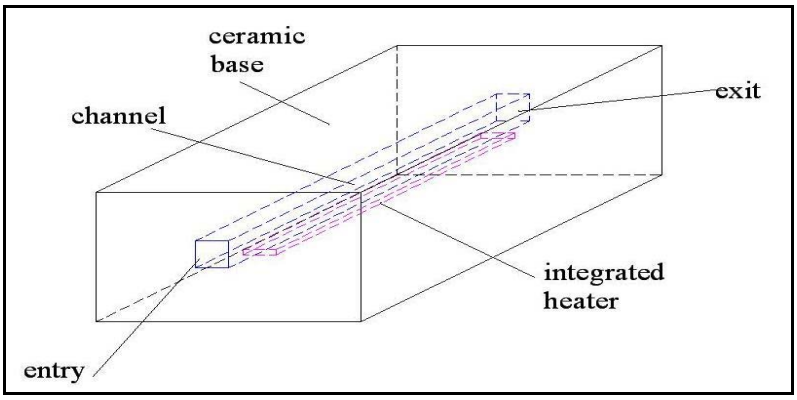



Figure 3.2: The modified model used for this thesis.

The integrated heater is an Ag-Pd heater (Sadler, et. al., 2003). An important aspect for the integrated heater is the generated heat. The generated heat (power) from the integrated heater was first maintained at 500mWatts (Sadler, et. al., 2003). There are two reasons for this decision. The first is to allow some tweaking and options to conduct an analysis to find a more suitable power value for a no-flow condition based on the modified model. The second reason was to find a common ground with the original model to start some trial and error procedures. These trial and error procedures were particularly important, especially since the literature didn't specifically mention the dimensions of the integrated heater's that were used in the

simulation. The literature also didn't specifically disclose the integrated heater's exact position. The trial and error procedures were performed until a reasonable dimension and position were found for the integrated heater based on a sensible temperature range for the DCS (in a no-flow condition of the modified model) and also the generated heat from the integrated heater itself. So the integrated heater is positioned closely (but not in contact) under the channel in a balance-centered manner. The gap between the top surface of the integrated heater and the bottom surface of the channel is 0.2mm while the heater's dimensions are 0.5mm (width) x 11mm (length) x 0.1mm (thickness).

The entire solid model was simulated and analyzed using ANSYS 8.0. The accuracy level of the simulation is dependent on the meshing by the ANSYS software. However some compromise among accuracy, simulation time, hardware and software limitation needed to be taken into consideration. In addition to that, it should also be mentioned that some scaling was required in the units before it can be accepted in ANSYS (Appendix A). Explanation on this is available in the ANSYS help files.

This single channel model provides more flexibility in the analyses using ANSYS. This includes the parameters changes, which is not very feasible for a 3-channel model. In addition to that, a single channel allows more focus on the thermal effects on the DCS (DNA cocktail solution) due to parameter and environment change, which is one of the main objectives in this thesis. Effects of these parameters changes can be conveniently observed and are more noticeable. Besides that the software and hardware limitation factor also plays some part for this choice. By understanding the basics on a single channel model, it can be applied on a complete 3-channel model. This single channel can be referred to as a fundamental approach in understanding the thermal effects on the DCS in a microfluidic channel.

## 3.3 Material Properties

The thermal and material properties used for the entire analysis are as follows: -

a) Ceramic base

   Sadler et. al. (2003) suggests the use of Dupont 951 (DuPont, 2002), a LTCC or Low Temperature Co-fired Ceramic. Information on LTCC can be found in Hsu, (2002), Tummala, Eds., (2001) and (DuPont, 2002). The properties of DuPont 951 are shown in Appendix B: Table B1.

b) DNA Cocktail Solution (DCS)

Sadler, et. al. (2003) didn't provide conclusive information on the properties of the DCS. Furthermore properties of DCS are dependent on the different variety of products available in the market and the specific DNA itself. A similarity among the different range of DCS is that it is predominantly composed of DNA-free distilled water. The properties of water are based from Holman, (2001) (Appendix B: Table B2). It should be reminded that although the concern of this thesis is the thermal effects to the DCS, it is however, limited by monitoring the effects under certain temperature ranges. Under these temperature ranges, the DCS and the denaturing process are expected to be at an optimal level. Hence the material properties for the DCS here should not be any consequence to the analysis.

c) Ag-Pd integrated heater

The integrated heater is made of Ag-Pd (Argentum-Palladium) substrate. However the properties of silver (Ag) from Callister Jr., (2000) were used instead since the properties of Ag-Pd alloy was unavailable. The properties of silver are shown in Appendix B: Table B3. It should be noted that in several trials it was found that material properties of the heater had no consequence to the analysis.

## 3.4 Analysis Terms And Concepts

Before proceeding further some concepts and terms first need to be clarified. Some figures are included will either be in 45$^{o}$ angle view or bottom view. This is dependent on the analysis and the one with a better view. The terms and concepts include: -

a) Optimal thermal zones

Optimal thermal zones are coloured contours that occur within the predetermined optimal temperature range. It is considered that DCS (and denaturing process) works most favorably within these zones. The conditions that will be usually observed are the coverage of these optimal thermal zones (Figure 3.3 and 3.4). Optimal thermal zones are also called optimal thermal areas or optimal thermal regions. Sometimes optimal thermal zones are also referred to as thermal zones, thermal areas or thermal regions.

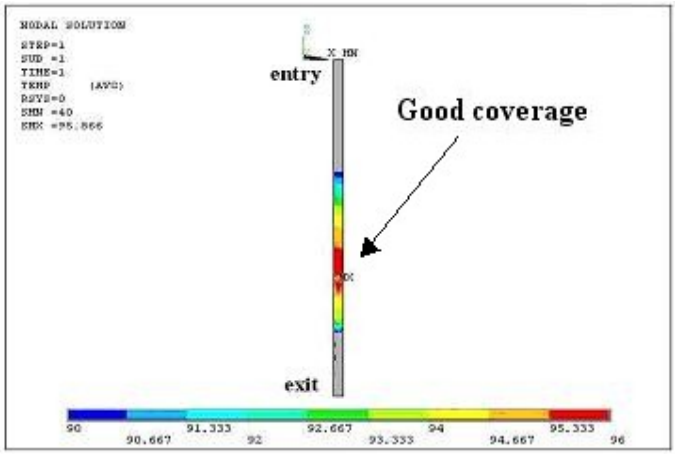



Figure 3.3: Optimal thermal zones with good coverage.

*[Note: This thermal zone (the colored contours) is for the Optimal Temperature Range of 90°C to 96°C. The entry and exit are always the same for figures from the bottom view.]*

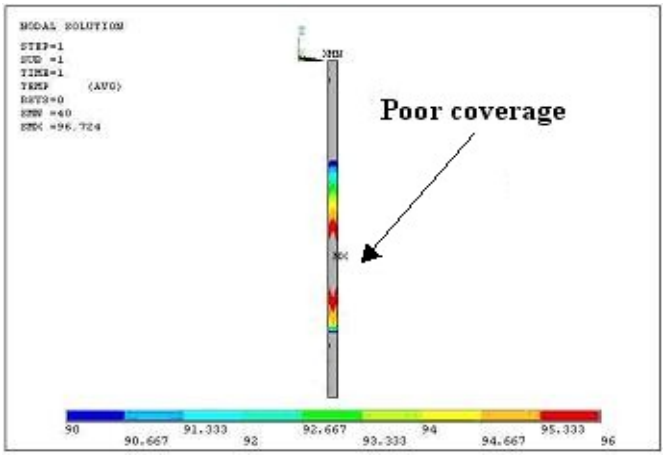



Figure 3.4: Optimal thermal zones with poor coverage.

*[Note: Observe the uncovered area in the hottest region that shows poor coverage.]*

b) Highest temperature range

Observe the most right corner of the legends for Figure 3.5. It can be noticed that the legends is coloured in red. This is the highest temperature range. All minimum and maximum temperature values of the highest temperature range

are presented in tables. It should be noted that the figures presented in this report do not use the type of figure shown in Figure 3.5. The reason for this is Figure 3.5 represents the overall thermal effects. It is used merely for obtaining the exact values of the highest temperature range. To get a specific view of the thermal zones, figures with contours of predetermined optimal temperature range are use instead. DCS can be damaged (and enzymes may breakdown) if the temperature values are too high. If temperature is too low, the denaturing process may not be optimal or not occur at all. Both situations will result in incomplete denaturing process. Hence data in the highest temperature range is important since it allows monitoring of the process.

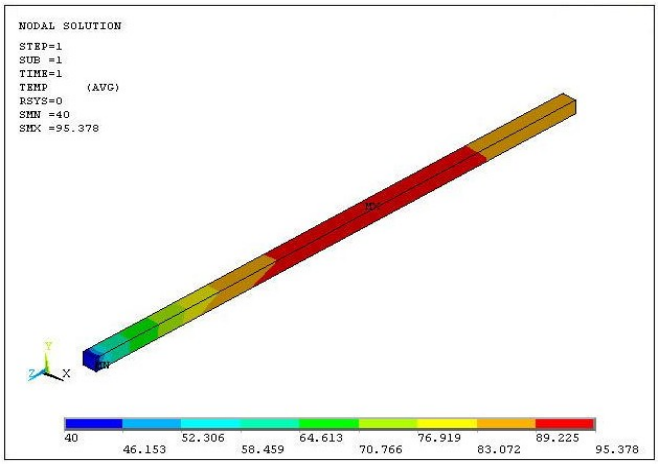



Figure 3.5: Overall thermal effects.

c) Optimal temperature range

Two optimal temperature ranges will be used. One is the 90ºC to 96ºC and the other 93ºC to 95ºC. The optimal temperature range will also be referred to as predetermined optimal temperature range. It is considered that DCS and the denaturing process work at an optimal level within this temperature range.

d) Split

A split is referred to a thermal zone breaking into two separate zones, which usually reduce the overall coverage (Figure 3.6). A split usually happens when the temperature in mid-region (where the heater is placed closely underneath

the channel) is higher than the predetermined optimal temperature range. When a split happens the trend usually shows that the separated zones move further apart to either ends of the channel while at the same time having reduced coverage of optimal thermal zones.

e) Temperature below range

This term is used when the thermal zones being studied are below the optimal temperature range hence causing no optimal thermal zones to appear. This is due to the fact that maximum value of the highest temperature range is below the minimum value of the optimal temperature range.

f) Temperature above range

This term is used when the thermal zones being studied are above the optimal temperature range hence causing no optimal thermal zones to appear. This is due to the fact that minimum value of the highest temperature range is above the maximum value of the optimal temperature range.

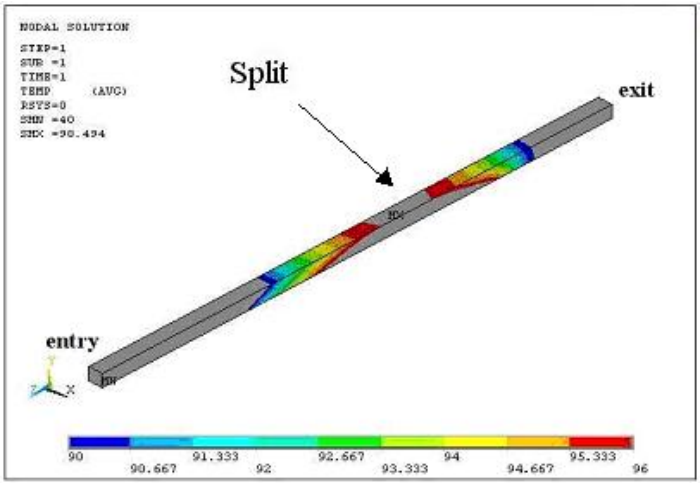



Figure 3.6: Occurrence of a split.

*[Note: The thermal zones break into 2 separate zones. The entry and exit are always the same for figures in this 45º angle view.]*

## 3.5 Criteria Of Optimal Thermal Conditions

Optimal thermal conditions are a situation where the best thermal zones are obtained for a particular analysis. Even though it is dependent on case-to-case basis but there are criteria that must be followed in determining optimal thermal conditions. The following are the criteria for optimal thermal conditions: -

a) No splits.
b) Best or maximum coverage of optimal thermal zones, possibly with no uncovered areas.
c) If possible the maximum value of the highest temperature range should not exceed the predetermined optimal temperature range.

## 3.6 Variation Of Heat Generated From Heater

The effect of heater power on the DCS (DNA cocktail solution) in the channel is a sensitive subject. This is mainly because there is difference between optimal heater powers in flow condition and no-flow condition. Sadler, et. al., (2003) presented optimal heater power for the denaturing process (in a flow condition) is at 500mW. In this analysis the optimal power for the suggested single channel model (in a no-flow condition) will be investigated. In addition, thermal effects of heater power variation on the DCS in the channel will be studied.

The integrated heater in the single channel model will be put through different range of powers. Starting from 400mW to 500mW with an increase of 10mW each time. It should be noted that ANSYS solution only recognizes heat generated per volume ($W/m^3$) and not merely the heat generated (W). However since the volume is not affected, only the heat generated will be observed at this stage. The results are summarized in Table 3.1 and Graph 3.1 is plotted. Results are discussed based on the plotted graph and the predetermined optimal temperature ranges.

### 3.6.1 Results For Variation Of Heat Generated From Heater Analysis

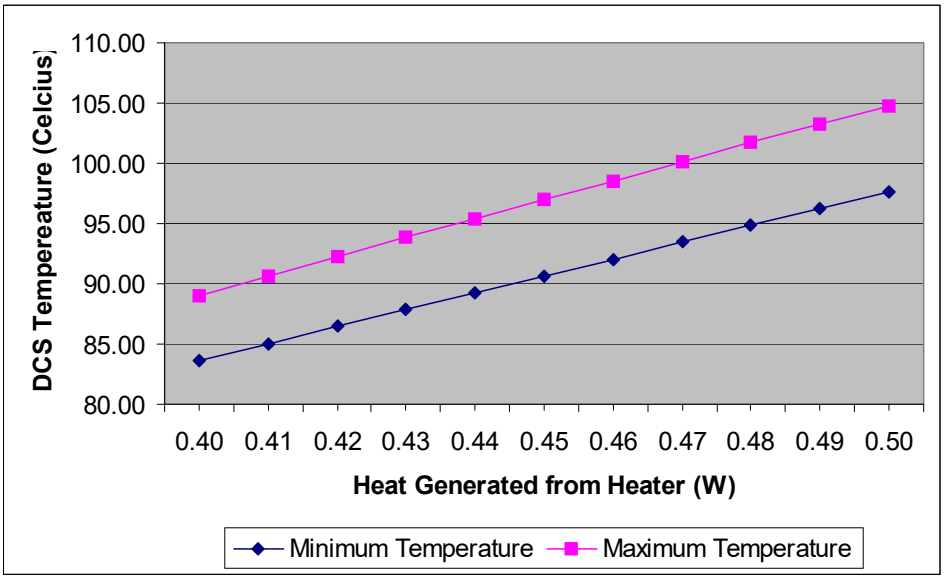
Table 3.1: Data from variation of heat generated from the heater analysis.

| No | Heat Generated (W) | Highest Temperature Range | | Observation/ Notes | |
|---|---|---|---|---|---|
| | | Minimum Temperature (°C) | Maximum Temperature (°C) | 90°C to 96°C Temperature Range | 93°C to 95°C Temperature Range |
| 1 | 0.40 | 83.61 | 89.06 | Temperature below range. | Temperature below range. |
| 2 | 0.41 | 84.99 | 90.62 | Small area at mid channel facing heater. | Temperature below range. |
| 3 | 0.42 | 86.46 | 92.26 | Previous area increasing, some coverage on the top area. | Temperature below range. |
| 4 | 0.43 | 87.84 | 93.82 | Optimal thermal zone increases rapidly, mostly ranging between 91°C to 94°C. Very good coverage. | Small area at mid channel facing heater. Fairly good coverage. Most of the optimal thermal zones ranging between 93.44°C to 93.89°C. |
| 5 | 0.44 | 89.23 | 95.38 | Optimal thermal zone increases marginally, mostly ranging between 91°C to 96°C. Very good coverage. | Optimal thermal zone increases marginally, mostly ranging between 93°C to 93.44°C. Less coverage. |
| 6 | 0.45 | 90.61 | 96.94 | Optimal thermal zone decreases rapidly, mostly ranging between 94°C to 96°C. Less coverage especially bottom area. | Area of optimal thermal zones decreases mostly ranging between 93.89°C to 94.78°C. Coverage decreases. |
| 7 | 0.46 | 92.00 | 98.49 | Split occurs. Coverage continues to decrease. | Split occurs. Coverage continues to decrease. |
| 8 | 0.47 | 93.46 | 100.14 | Coverage continues to decrease. The 2 split thermal zones move to either end of the channel. | Coverage continues to decrease. The 2 split optimal thermal zones move to either end of the channel. |
| 9 | 0.48 | 94.84 | 101.70 | Coverage continues to decrease. The 2 split thermal zones continue to move to either end of the channel. | Coverage continues to decrease. The 2 split thermal zones continue to move to either end of the channel. |
| 10 | 0.49 | 96.23 | 103.25 | One thermal zone concentrates at the exit with most zones ranging between 90°C to 92°C. Other split area exists but less coverage. | One thermal zone concentrates near the exit. Other split area exists but coverage decreases. |
| 11 | 0.50 | 97.61 | 104.81 | One thermal zone concentrates at the exit with most zones ranging between 91°C to 94°C. Other split area exists but less coverage. | One thermal zone concentrates near the exit but area decreases. Other split area exists but coverage decreases. |

### 3.6.2 Discussion For Variation Of Heat Generated From Heater Analysis

Graph Analysis

From Graph 3.1, shows DCS temperature against heat generated from heater. It shows that a linear relationship can be obtained between the two values investigated. As the DCS temperature increases, the minimum and the maximum values of the heat generated from the heater also increases. The minimum line (considered from 0.40W to 0.50W) shows an increase of 16.74% while the maximum line (considered from 0.40W to 0.50W) shows an increase of 17.68%. The increase in these minimum and maximum lines gives an average of 17.21%. So based on this average, Graph 3.1 shows that mere increase of 0.01W is capable of increasing the temperature of the DCS to almost 2°C (exact value is 1.72°C).




Graph 3.1: DCS temperature vs. heat generated from heater.

Analysis of the 90°C to 96°C Optimal Temperature Range

From the variation of heater power between 0.40W to 0.50W, only 0.40W didn't show any occurrence of optimal thermal zones. This is possibly due to the maximum temperature being below the minimum of the 90°C to 96°C Optimal Temperature Range. Between 0.41W to 0.44W optimal thermal zones shows an increasing trend. It

is at 0.44W that optimal thermal zones fulfill the criteria of the optimal thermal conditions (Figure 3.7).

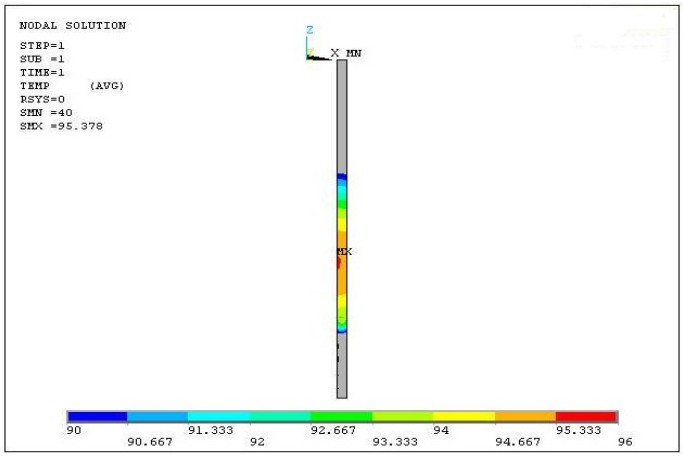



Figure 3.7: At 0.44W, optimal thermal zones fulfill the criteria of optimal thermal conditions.

However between 0.45W to 0.48W, the optimal thermal zones shows a dwindling trend, with a split occurring at 0.46W. Optimal thermal zones move to either ends of the channel showing a possibility that the temperature exceeds the 90$^{o}$C to 96$^{o}$C Optimal Temperature Range in the mid region of the channel. Finally between 0.49W to 0.50W the trend shows an increasing coverage and concentration of optimal thermal zones at the exit end of the channel. However its overall coverage (at these 0.49W to 0.50W) is still much smaller compared to what was seen at 0.44W. As shown in Figure 3.8, the distance of the split thermal zones are far apart. This possibly indicates that the area in between has a temperature above the maximum value of 90$^{o}$C to 96$^{o}$C Optimal Temperature Range. It is noted that between the values of 0.46W to 0.50W, the thermal zones do not fulfill the criteria of optimal thermal conditions.

Analysis of the 93°C to 95°C Optimal Temperature Range

This temperature range shows similar characteristics to the 90°C to 96°C Optimal Temperature Range. The main differences are: -

a) It took a much higher heater power (at least 0.43W) to raise the temperature to reach its minimum level.
b) Areas of the optimal thermal zones (for 93°C to 95°C Optimal Temperature Range) are much smaller in coverage size compared to the 90°C to 96°C Optimal Temperature Range.

At 0.44W, the optimal thermal zones are evaluated as the best. So the optimal power of the integrated heater for this optimal temperature range is also at the 0.44W.

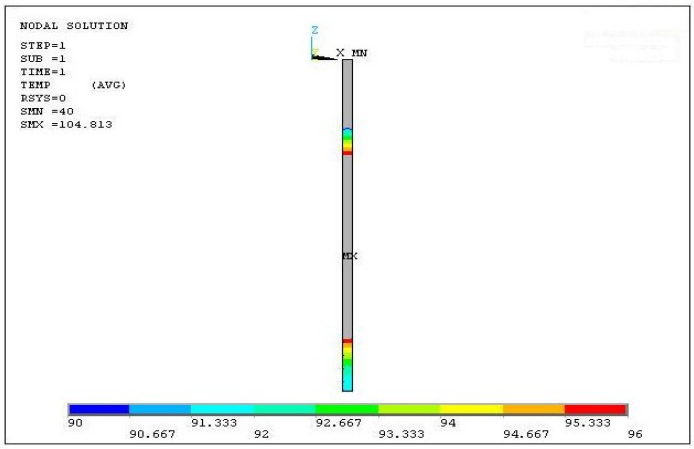



Figure 3.8: At 0.50W, optimal thermal zones shows increase of coverage and concentration at the exit end of the channel.