SIMULATION BASED DESIGN OF A THERMOELECTRIC COOLER FOR PCR-THERMAL BLOCK

Muhammad Ejaz[1], Zafar Bangash[1], Imran Raouf Malik[2], Imran Akhtar[1]
[1]College of Electrical and Mechanical Engineering,
National University of Sciences and Technology,
Islamabad, Pakistan.
[2]Foundation University, Islamabad, Pakistan.
Corresponding Author Email: muhammad.ejaz18@me.ceme.edu.pk

Abstract:

The static chamber microfluidic device (thermal cycler) is a laboratory apparatus of crucial significance in the field of biomedical sciences, especially its use in medical diagnostics. For effective and correct progression of the polymerase chain reaction, the temperatures corresponding to each step of the reaction must be controlled precisely. To that end, a thermoelectric cooler (TEC) is attached to the microfluidic device for heating and cooling of the thermal block of microfluidic device to achieve temperature for three steps PCR which is denaturation, annealing, and extension. Using TEC, temperature required for PCR (95, 55, and 75^oC) is achieved at the top plate which is transferred to the sample block to heat and cold down the sample fluid. The temperature response of polymerase chain reaction is compared with the temperature response of CFX Bio-Rad, and we find out that ramp rate from our analysis give better accuracy with a large hold or length of time. Additionally, the thermal methods prescribed herein are equally applicable to other thermoelectric coolers as well.

Keywords
Polymerase chain reaction (PCR); Thermoelectric cooler; Sample block; Numerical simulation.

Introduction:

Since its invention in the 1980s, polymerase chain reaction (PCR) has become one of the most widely used laboratory procedures for DNA amplification for scientists and doctors to study it in detail. The pathogen's in DNA are often detected using PCR techniques [1][2] . The DNA are very sensitive, PCR are used to identify specific sequence variants which are exact strain causes sickness. The PCR is basically perform using thermal cycling by heating and cooling that DNA mixture. PCR is performed in three steps and each step has its own temperature range as Denaturation ($92-98^o$C), annealing ($50-60^o$C) and extension ($68-75^o$C). The key element for a successful PCR is to control temperature and achieving that temperature for these three steps of PCR [3][4][5]. Set-ups that are more sophisticated have been presented by Khandurina *et al.* [6] who have created a system that consists of a Peltier-based compact heat cycling assembly around a microchip gel electrophoresis platform for quick PCR-based analysis.

Different techniques which are used to control these steps are thermoelectric module (Peltier device) [7] [8] [9], resistive patterned heater which is called thin-film heater [10] [11], an infrared radiations for non-contact reaction mixture [12], and heating through microwaves [13]. Robert de Saint Vincent et al. [14] used a laser as a heating source in their research. Using an inverted microscope, the researchers focused a continual Argon-ion laser (wavelength in vacuum 0 = 514.5 nm) on a PDMS microchannel. 0.1 percent fluorescein is added to the aqueous phase to heat it up. A thermoelectric module can also be used as a thermoelectric generator to generate electric power if temperature difference is maintained at its ceramic plates. But for this study it is used as a thermoelectric cooler (TEC) and used to produce heating, cooling, and energy by varying electric current as an input. From all these techniques thermoelectric (TE) module is studied here numerically for heating and cooling of thermal block. The thermoelectric cooler are used in a broad array of applications owing to its small size, low weight, high accuracy, and integrated heating and cooling capabilities, such as microelectronic systems, telecommunication, space ships and biomedical devices [15][16]. Another advantage of using TEC module in microfluidic device is that it comes in low cost as compared to other techniques which are mentioned earlier, which will reduce the cost of diagnostic test. In this study thermal block is taken from Raza *et al.* [17] and a simulation-based material test is performed for the thermal block by taking aluminium copper and gold material to select one that has good temperature response and is cost effective. and design a thermoelectric cooler for it, to give proper thermal cycle for PCR. Here for a PCR reaction to perform three different temperature is achieved which is 95, 55, and 75^oC at the top plate of TEC module in steady state at some input current values. The thermal block is then attached at the top plate of TEC, and the three set temperature values which was achieved first at the top plate of TEC is now obtained for the sample fluid, which is present in the polypropylene tube of thermal block. The thermal block and TEC module assembly is simulated in transient thermal module also to see the transient temperature response of sample fluid. The sample fluid temperature response of CFX Bio-Rad, which is run for denaturation step of PCR only for 25 sec of a cycle, is compared with our transient results.

Physical model:

Thermoelectric cooler which is also called Peltier module, include different material like ceramic plates, nickel plates as a diffusion barrier, solder, copper plates, and Bi_2Te_3 material is used as p and n-type semiconductor pellets are soldered on copper plate. Total 65 pairs of p and n type semiconductors or thermocouples are connected thermally in parallel and electrically in series between the ceramic plate and which is shown in Figure 1. The copper plate used here is to join these thermocouples with each other. The current is an input to the TEC module at one end of a copper plate. Movement of charge from copper plate through TEC module generates heat at top side and cools bottom ceramic plate. The TEC module geometry is made in SOLIDWORKS which is then imported in the ANSYS for simulation. The dimensions of TEC module is shown in Table 1.

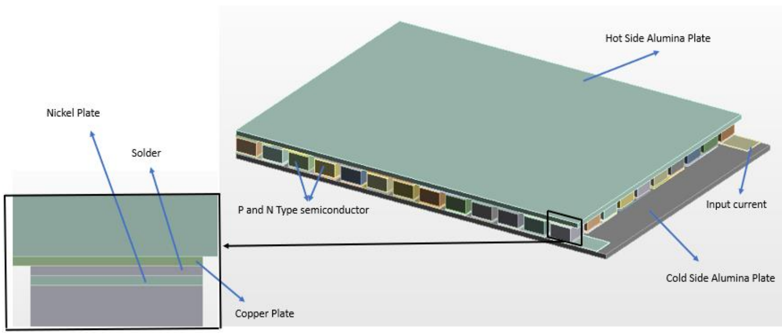

Figure 1 Schematic of thermoelectric cooler

Table 1 Thermoelectric cooler module parameters

Parameters	**Dimensions**
Copper, solder, and nickel plate thickness	0.1 mm
Ceramic plate thickness	0.64
Pellet length	1.78 mm
Pellets cross sectional area	3×3 = 9 mm^2
Distance between pellets	.85 mm

Table 2 Thermoelectric cooler module material properties [18] [7]

	Density (kg/m³)	**Specific Heat** (J/kg °C)	**Isotropic Thermal Conductivity** (W/m. °C)	**Isotropic Resistivity** (Ω m)	**Isotropic electrical conductivity** (Simons/m)	**Isotropic See beck Coefficient.** (V/°C)
Bismuth telluride (Bi2Te3) (n-type semiconductor)			1.2	1.05E-05		-0.000165
Bismuth telluride (Bi2Te3) (p-type semiconductor)			1.2	9.8E-06		0.00021
Nickel (Diffusion barrier)	8900	444	91.74	6.8966E-08	1.45E+07	
Alumina (Ceramic plate)	3800	880	14			
Solder	8000	167	48	1.4286-07	7+06 S	
Copper	8940	385	401			

Peltier Mesh Independence:

The computational domain taken here is consisted of 178850 hexahedron elements and 1138917 nodes. Cooling capacity (Q_c) which is heat load at the cold plate of TEC module and the heat load at the hot plate (Q_h) of TEC module which is the heat that is pumped from the cold plate, changes with decreasing mesh size which is plotted in Figure 2 and **Error! Reference source not found.**. The simulation is run for four different mesh sizes while making the boundary condition constant for all mesh sizes which are convection coefficient $h = 3\, W/m^2.\, ^oC$ and ambient temperature $T_{ambient} = 22\, ^oC$. The input current values which are 3.005 amp for achieving denaturation temperature, 2 amp for annealing temperature and 2.55 amp for achieving extension temperature. These current values also constant for all mesh sizes. The last two values in Figure 2(a) and (b) for all three curves of denaturation, annealing and extension showed very less sensitivity toward mesh sizing. Mesh with 178850 elements is selected and further decrease in mesh size is stopped. Figure 3 shows meshing of thermoelectric cooler.

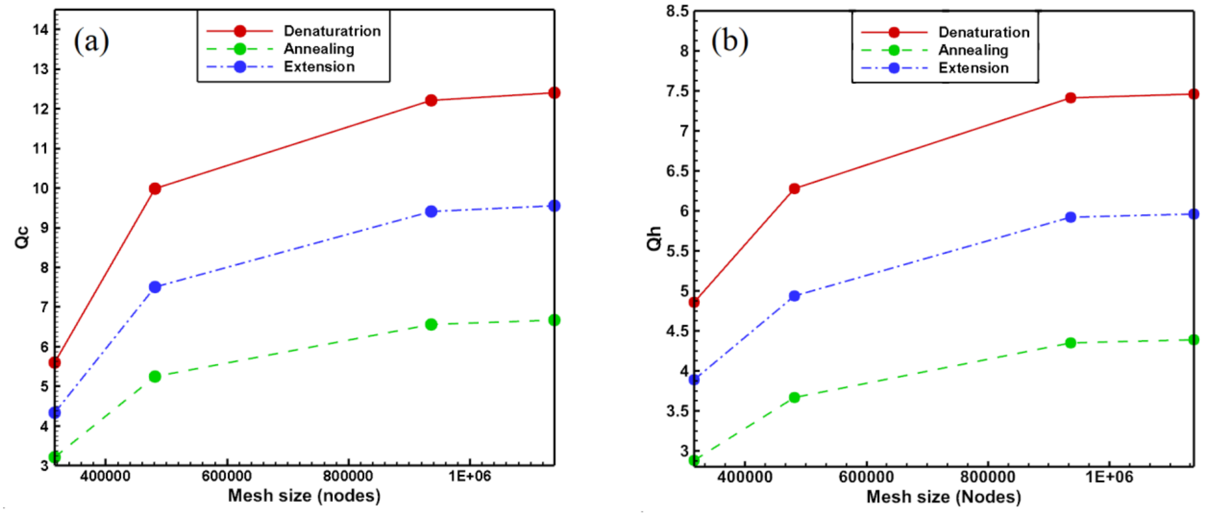

Figure 2: (a) Q_C vs Mesh size. (b) Q_h vs Mesh size

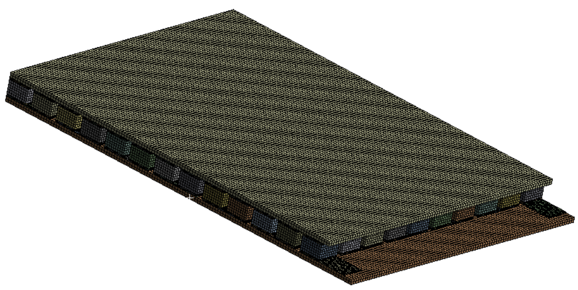

Figure 3: TEC module Mesh

Thermoelectric cooler simulations results:

Steady state finite element analysis is performed in Thermal Electric module of Ansys, in which three current values is given as a input to the TEC module to obtain three different temperatures at the top plate of TEC module. These three temperature values are for denaturation, annealing and extension step of polymerase chain reaction (PCR) which is 95, 55 and 75^oC respectively. The maximum heat load (Q_c, Q_h) at the top and bottom surface TEC module is taken here. The inputs to simulation are current, convection coefficient and ambient temperature (22 °C). In Table 3 ΔT is the temperature difference between hot and cold plate of TEC module, V is the voltage that ANSYS gives as a output, h is the natural convection coefficient that is given to the TEC module as a boundary condition.

Table 3 : Numerical simulation results of TEC module

Current(Amp)	h(W/m^2.°C)	Q_c(Watt) bottom surface	Q_h(watt) Top surface	T_c (°C)	T_h (°C)	ΔT (°C)	V (volts)	COP
3.005	3	12.21	7.43	62	95.055	33.055	1.6286	2.55
2	3	6.56	4.371	35.99	55.78	19.79	1.0316	3.09
2.55	3	9.40	5.9	48.4	75.01	26.61	1.3475	2.68

$$\mathrm{COP} = \frac{\mathrm{Q_c}}{\mathrm{W}} \quad (1)$$

$$W = Qh - Qc \quad (2)$$

$$W = VI \quad (3)$$

In equation (1) the coefficient of performance (COP) is defined as the ratio of heat capacity Q_c or removal of heat from cold junction to the total energy that used by the TEC module and power across the thermocouples W (p and n-type semiconductors) of TEC module. In equation (2) Qh is the heat load that is absorbed by the hot plate of TEC module. In Table 3 : Numerical simulation results of TEC module, it is shown that with the increase of COP the cooling Capacity $\mathrm{Q_c}$ is increased for a given current. It means that if we decrease the cold and hot side temperature difference the COP will increase. In equation 3, W is the Electric Power generated from thermocouples of TEC module, V is the voltage that ANSYS give out as an output for input which are current I and convection coefficient. In Table 4 the generated electric power is calculated using equation 2 and 3, which is same with error which is below 10 percent, so it shows that the thermal finite element model which we setup is accurate with some error. Figure 4 is the snap shot of TEC module temperature contours at the denaturation stepp.

Table 4 Thermoelectric cooler module material properties

Current (Amp)	W=Q$_h$-Q$_c$	W=VI
3.005	4.78	4.893
2	2.19	2.06
2.55	3.5	3.43

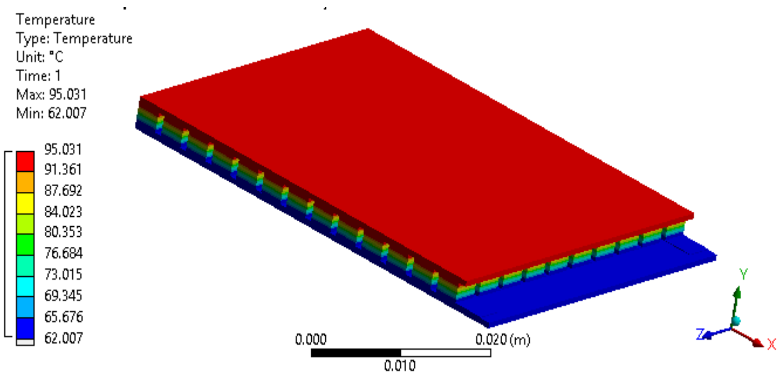

Figure 4: Temperature response of Thermoelectric cooler

Thermoelectric cooler hot and cold plate temperature response:

Three different mesh sizes are taken here to accurately obtain temperature for three steps of PCR which are 95, 55 and 75 ^oC using thermoelectric cooler. Numerical simulations of TEC are performed by changing mesh sizes while input current values and other boundaries conditions are taken as constant are shown in **Error! Reference source not found.**, in contour A,B, and C with the increase of mesh elements the temperature increased, and at the last two mesh sizes the change is less than 1% so we stop further increase in mesh elements . If we look to the non-uniform temperature distribution on the cold plate of TEC, so with the increase of mesh elements the spots of the plate at which the copper plate straps are attached, became more visible. Just like the cold plate, the hot plate temperature also increased with the increased in mesh elements and the temperature distribution on hot plate due to copper plate became more visible which is shown in D, E, and F of Figure 5.

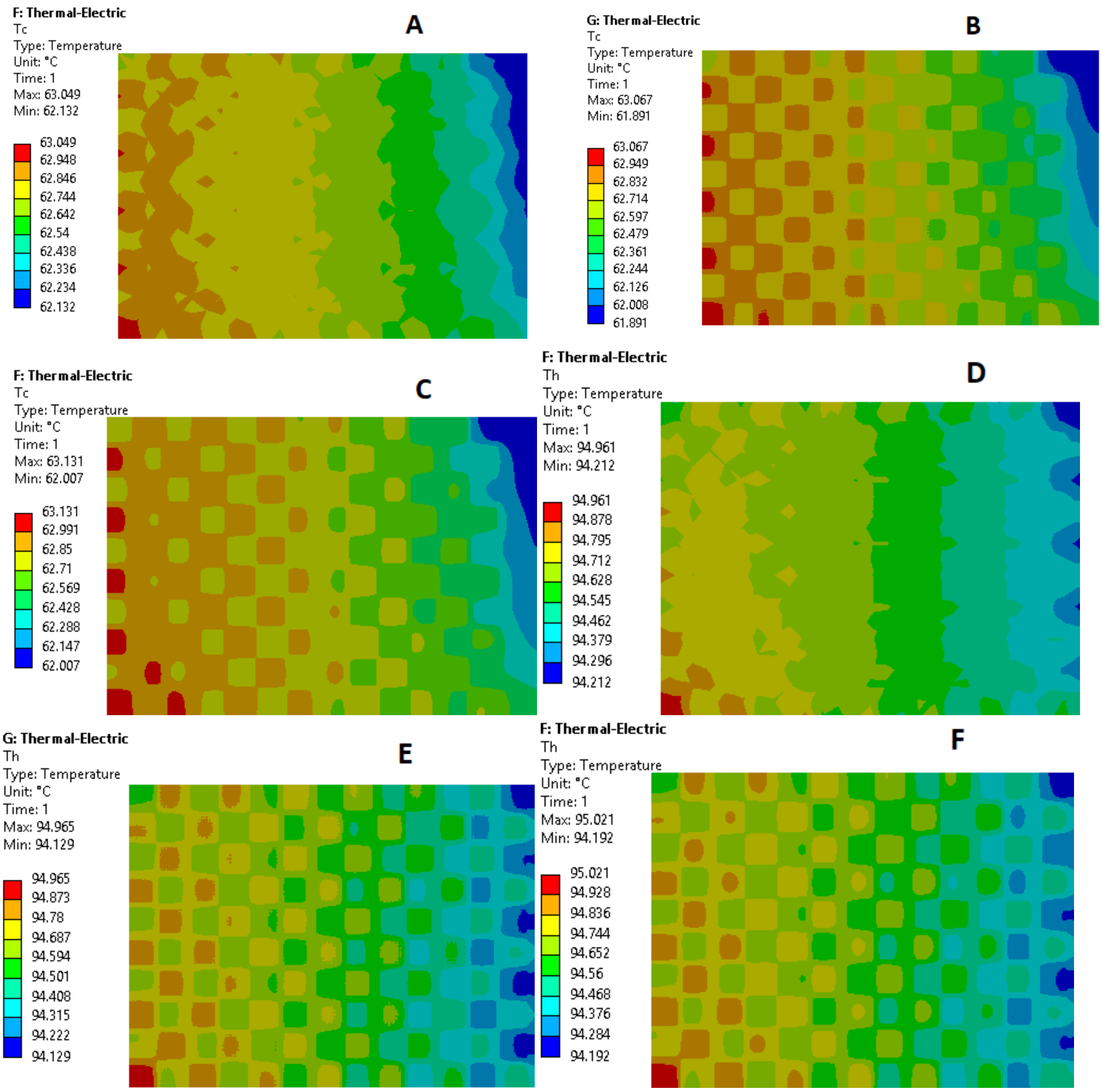

Figure 5: *Temperature contours of cold and hot plate of Thermoelectric cooler at different mesh sizes and at: I = 3.005 A,* $h = 3\,W/m^2.\,^oC$ *and* $T_{ambient} = 22\,^oC$*.(A) Cold plate with 41902 elements and 315455 nodes (B) Cold plate with 163578 elements and 936060 nodes (C) Cold plate with 178850 elements and 1138917 nodes (D) Hot plate with 41902 elements and 315455 nodes € Hot plate with 163578 elements and 936060 nodes (F) Hot plate with 178850 elements and 1138917 nodes.*

Material for thermal block:

Thermal block is simulated in transient module of ANSYS using finite element analysis, to investigate the thermal response of different materials for thermal block. Three different temperatures are given as a boundary condition at the base of thermal block which is 95, 55 and $75^{o}C$, the time for each temperature is 15 sec and for the whole PCR cycle is 45 sec. The fluid on which the PCR rection is perform is taken here as a water, present in a polypropylene tube and these tubes are then put in the thermal block which is heated and cold down. Ambient temperature taken here as $22^{o}C$ and convection coefficient for thermal block taken as 1 $W/m^{2}.\ ^{o}C$. Here the mesh size, convection coefficient and temperature, all are same. The only thing we change is its materials. We simulate the thermal block for aluminium, gold, and silver, in these 3 materials the temperature response of gold is better from silver and aluminium, as shown in Figure 6 gold achieve the set temperature at the denaturation and extension step at a high ramp rate than silver and aluminium, but gold is not cost effective so aluminium material is selected because it is cost effective and have good temperature response than silver. Figure 7 shows the temperature contours of aluminium thermal block for denaturation step at a time of 13 sec.

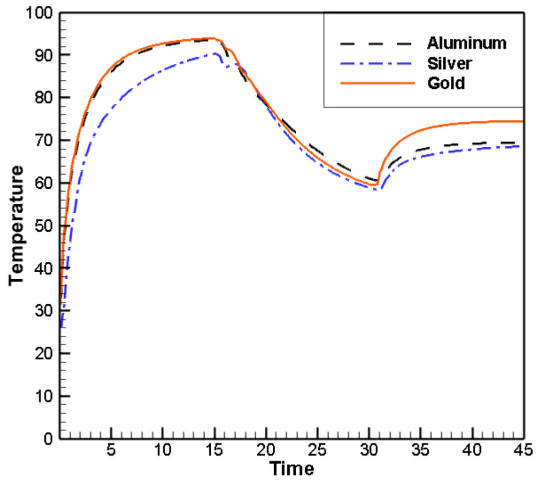

Figure 6: Temperature response of fluid for different thermal block materials

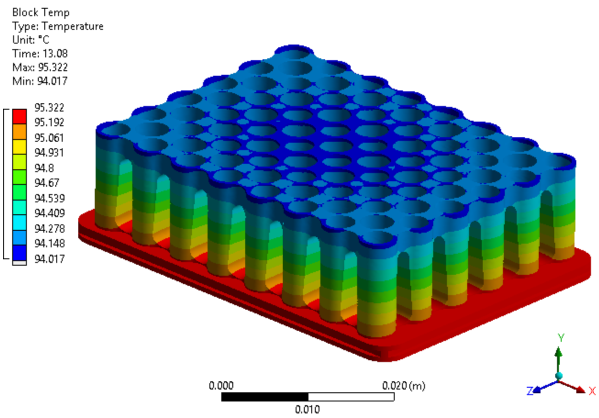

Figure 7: Temperature response of thermal block

TEC module and thermal block numerical modelling:

Hot plate of thermoelectric cooler is attached with the bottom of thermal block, because the heat is transfer first from the hot plate to the bottom then from bottom of thermal block to the polypropylene tubes and then to fluid which is present in the tube. After attaching TEC module, steady state numerical simulation is performed, in which three current values and the natural convection coefficient which is given as a input and shown in Table 5, at these input values the 95, 55 and 75 ^oC is obtained on the hot plate of TEC and which is then transfer to the sample fluid. The simulation is also run in the transient module of ANYS, as in this module there is no current option the heat flux $(Q_c \ and \ Q_h)$ is given as a input on the cold and hot plate of TEC module which is obtained for input current values in the steady state thermal electric analysis for the hot and cold plate of TEC module given in Table 5. The time for each step in PCR is 15 seconds, so in transient module each $Q_c \ and \ Q_h$ value which would produce 95 ^oC for first step, 55 ^oC for second step and 75 ^oC for third step, is given as a input for 15 seconds for each step. The average heating ramp rate (up ramp) for denaturation step is 6.36 $^oC/W$ with 5 sec hold time, the average cooling ramp (down ramp) for annealing is 6.18 $^oC/W$ with a hold time of 3 sec and at last the average heating ramp for the extension step is 3.3 $^oC/W$ with a hold time of 11 sec.

Table 5 Numerical results of TEC module and thermal block assembly

Current(Amp)	h(W/m^2.^{o}C)	Q_c(Watt) bottom surface	Q_h(watt) Top surface	T_c (^{o}C)	T_h (^{o}C)	ΔT (^{o}C)
3.25	3	9.99	5.05	61.44	95.21	33.77
2.13	3	5.33	2.74	34.71	54.81	20.10
2.68	3	7.41	3.75	45.87	72.24	26.37

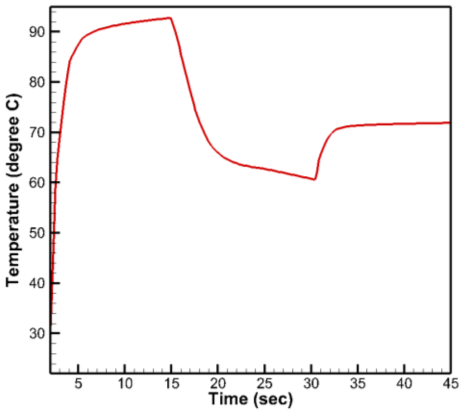

Figure 8: Temperature response of fluid.

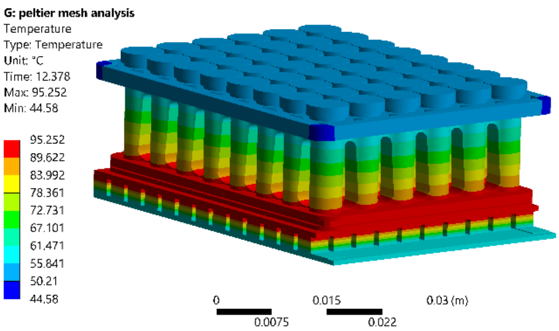

Figure 9: Temperature contour of TEC module and Thermal block

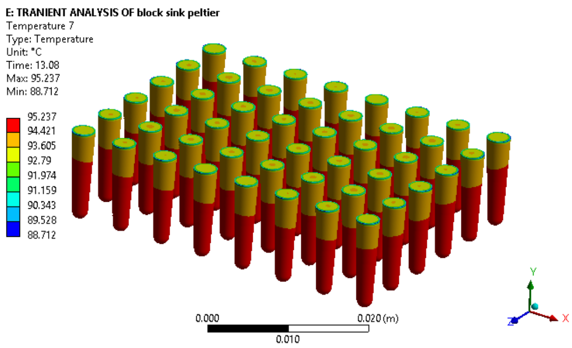

Figure 10: Temperature contours of fluid

Comparison:

In this study the temperature response of sample fluid is compared with CFX Bio-Rad given in [1]. The comparison shown in the Figure 11 between the temperature response of present study and CFX Bio-Rad shows that both the studies achieves the set temperature of denaturation step which is $95\ ^oC$, while the length of time or hold time of present study is larger than CFX Bio-Rad device, also the present study achieve the set temperature with a high ramp rate.

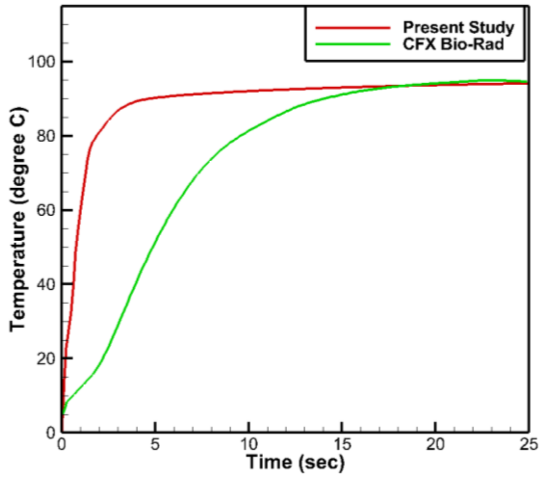

Figure 11: Temperature response comparison of denaturation step of PCR

Conclusion:

This paper presents the numerical modelling of thermoelectric cooler using finite element analysis. TEC module is studied numerically using steady and transient module of ANSYS. Here the TEC module is used for heating and cooling of a sample fluid to perform PCR reaction. The success or failure of PCR reaction depends on the accuracy of temperature response, and here the set temperature is achieved with a high ramp rate and good hold time or length of time. The up ramp rate for denaturation step is $6.36\ ^oC/W$ with 5 sec hold time, the down ramp for annealing is $6.18\ ^oC/W$ with a hold time of 3 sec and at last the up ramp for the extension step is $3.3\ ^oC/W$ with a hold time of 11 sec.

References:

[1] I. Raouf Malik, “Point of Care Molecular Diagnostics for Humanity,” 2014, [Online]. Available: https://thesis.library.caltech.edu/8494/1/POC MDx FOR HUMANITY.pdf.

[2] J. S. Kochhar, S. Y. Chan, P. S. Ong, W. G. Lee, and L. Kang, *Microfluidic devices for drug discovery and analysis*. Woodhead Publishing Limited, 2013.

[3] S. P. Selvaraj, V. Logasundari, and K. Kumaresan, “Temperature Control for PCR Thermo Cycler based on Peltier-Effect Thermoelectric,” *Test Eng. Manag.*, vol. 83, pp. 14303–14308, 2020.

[4] L. Thermal and S. Application, “Thermoelectric Modules Accelerate PCR Thermal Cycling,” no. July, 2017.

[5] S. Jeong *et al.*, "Portable low-power thermal cycler with dual thin-film Pt heaters for a polymeric PCR chip," *Biomed. Microdevices*, vol. 20, no. 1, 2018, doi: 10.1007/s10544-018-0257-9.

[6] J. Khandurina, T. E. McKnight, S. C. Jacobson, L. C. Waters, R. S. Foote, and J. M. Ramsey, "Integrated system for rapid PCR-based DNA analysis in microfluidic devices," *Anal. Chem.*, vol. 72, no. 13, pp. 2995–3000, 2000, doi: 10.1021/ac991471a.

[7] T. Gong *et al.*, "Numerical simulation on a compact thermoelectric cooler for the optimized design," *Appl. Therm. Eng.*, vol. 146, no. 122, pp. 815–825, 2019, doi: 10.1016/j.applthermaleng.2018.10.047.

[8] E. E. Antonova and D. C. Looman, "Finite elements for thermoelectric device analysis in ANSYS," *Int. Conf. Thermoelectr. ICT, Proc.*, vol. 2005, pp. 200–203, 2005, doi: 10.1109/ICT.2005.1519922.

[9] J. Huang, Z. Chen, and K. Hu, "FEA for steady-state thermal performance of PCR thermal-cycler based on thermoelectric cooler," *Proc. - 2011 4th Int. Conf. Biomed. Eng. Informatics, BMEI 2011*, vol. 2, no. Fig 2, pp. 1097–1100, 2011, doi: 10.1109/BMEI.2011.6098422.

[10] G. V. Kaigala *et al.*, "An inexpensive and portable microchip-based platform for integrated RT-PCR and capillary electrophoresis," *Analyst*, vol. 133, no. 3, pp. 331–338, 2008, doi: 10.1039/b714308g.

[11] M. Imran and A. Bhattacharyya, "Thermal response of an on-chip assembly of RTD heaters, sputtered sample and microthermocouples," *Sensors Actuators, A Phys.*, vol. 121, no. 2, pp. 306–320, 2005, doi: 10.1016/j.sna.2005.02.019.

[12] B. C. Giordano, J. Ferrance, S. Swedberg, A. F. R. Hühmer, and J. P. Landers, "Polymerase chain reaction in polymeric microchips: DNA amplification in less than 240 seconds," *Anal. Biochem.*, vol. 291, no. 1, pp. 124–132, 2001, doi: 10.1006/abio.2000.4974.

[13] J. J. Shah *et al.*, "Microwave dielectric heating of fluids in an integrated microfluidic device," *J. Micromechanics Microengineering*, vol. 17, no. 11, pp. 2224–2230, 2007, doi: 10.1088/0960-1317/17/11/008.

[14] M. Robert *et al.*, "Laser Switching and Sorting for High Speed Digital Microfluidics To cite this version : HAL Id : hal-00389849 Laser Switching and Sorting for High Speed Digital Microfluidics," 2009.

[15] P. N. Ngatchou *et al.*, "A real-time PCR analyzer compatible with high-throughput automated processing of 2-µL reactions in glass capillaries," *IEEE Trans. Autom. Sci. Eng.*, vol. 3, no. 2, pp. 141–150, 2006, doi: 10.1109/TASE.2006.871479.

[16] C. D. Ahrberg, A. Manz, and B. G. Chung, "Polymerase chain reaction in microfluidic devices," *Lab Chip*, vol. 16, no. 20, pp. 3866–3884, 2016, doi: 10.1039/c6lc00984k.

[17] M. Raza, I. R. Malik, and I. Akhtar, "Design and Thermal Analysis of Sample Block PCR for DNA Amplification," *Proceedings of 2020 17th International Bhurban Conference on Applied Sciences and Technology, IBCAST 2020*. pp. 210–217, 2020, doi: 10.1109/IBCAST47879.2020.9044508.

[18] R. McCarty, "A comparison between numerical and simplified thermoelectric cooler models," *J. Electron. Mater.*, vol. 39, no. 9, pp. 1842–1847, 2010, doi: 10.1007/s11664-010-1075-x.