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TC-PLUS Application note: A01-004B

Innovative Thermal Energy Recovery System (TERS®): A novel mechanism for controlling thermal cycler blocks

Introduction

Thermo electric coolers, also known as Peltiers, have long been used as the mechanism by which instruments such as thermal cyclers control the temperature of the blocks holding the reaction vessels. The precise way in which they can be controlled is essential for specific processes such as PCR. The current trend for rapid PCR cycling requires even faster heat exchange processes to occur without compromising the uniformity specification of the block. In this article we introduce the TERS® system of the Techne TC-PLUS thermal cycler which uses a novel energy saving mechanism to improve the ramp rates of a standard aluminium thermal cycler block.

Figure 1: The TC-PLUS thermal cycler with three satellite units. The TC-PLUS features a colour touch screen interface and unique space-saving stackable design. Up to nine satellite units can be controlled from a TC-PLUS, or alternatively can be controlled using PC software.

Rapid Cycle PCR

In the modern laboratory, speed is often of the essence and any process capable of saving valuable research time is an advantage. An increasingly popular technique in this direction, with many recent new products on the market, is that of fast PCR. Rapid cycle PCR was in fact developed around 20 years ago with the invention of hot air thermal cyclers (1). Samples were placed in thin glass capillary tubes and subjected to cycles of hot and cold air. The rapid heat transfer meant that PCR products could be amplified in as little as 15 minutes. More recently, advances in block technology have seen the introduction of conventional thermal cyclers capable of temperature ramp rates of up to 15ºC/second.

Ramp Rates and Fast PCR Protocols

The factors that determine the length of a PCR run include the number of steps and cycles (including any initial denaturation/enzyme activation and final extension steps), the hold times of these steps and the ramp rates between them. Ramp rates are an important part of the PCR as primer annealing and product extension will occur during these phases. Simply accelerating the ramp rate for heating and cooling of a PCR run without changing other program parameters can greatly reduce the total run time without compromising on sensitivity (Figure 2).

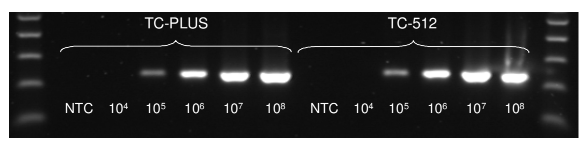

Figure 2: A 231bp fragment of the pBR322 plasmid vector was amplified in parallel in both TC-PLUS and TC-512 thermal cyclers, which have maximum heating ramp rates of 5.0ºC/s and 3.6ºC/s respectively. The numbers shown are the copies of template added to each 20µl reaction. NTC is a no template control. For this particular reaction, the results demonstrated no appreciable differences in yield or sensitivity between the two thermal cyclers. The program took approximately 1 hour to complete when using the TC-PLUS compared to 1h 30 min in the TC-512; a saving of around 30 min on the run time entirely due to the increased ramp rate of the TC-PLUS.

Fast PCR protocols on the other hand rely on greatly reducing the hold times for denaturation and elongation steps. Without proper optimisation and the use of specifically formulated reagents, which contain specialised enzymes and stabilisers to facilitate rapid ramping and short hold times, the reactions can show a loss of sensitivity and increased variability (2).

Traditionally, block thermal cyclers have used expensive gold-plated silver blocks in order to achieve the required rapid ramping speeds demanded by users. Silver has the highest thermal conductivity of any metal but has the tendency to tarnish in air so is therefore coated in gold, also with a high thermal conductivity, but resistant to oxidative corrosion. Traditional aluminium blocks have only about half the thermal conductivity of silver and are therefore more limited in ramp rate, especially the larger 96-well block formats. The TERS® system developed for the Techne TC-PLUS thermal cycler uses a unique means of controlling the thermal energy dissipated by the heat sink to offer an improvement in ramp rates compared to conventional aluminium blocks. The result is a ramp rate comparable to silver blocks but with better block uniformity and lower cost.

Thermo Electric Coolers (TECs)

TECs, or Peltiers, are semiconductor devices that transfer energy from one face to the other when a DC current is passed through them; this phenomenon is known as the Peltier effect. The direction of energy transfer is reversed when the applied current is reversed. The face of the device that energy is pumped from is known as the cold side and the face that energy is transferred to is known as the hot side (Figure 3).

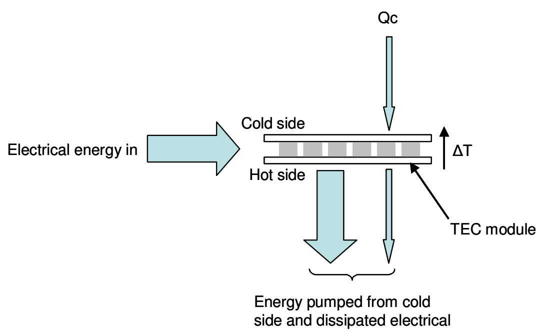

Figure 3: Definition of some terms relating to operation of a TEC. Qc is the amount of thermal energy pumped from attached objects e.g. thermal cycler well plate. ΔT is the difference in temperature between the hot side and the cold side of the TEC.

Any energy dissipated by the TEC is pumped to the hot side of the device. The amount of energy the TEC can pump from the cold to hot side, Qc, varies with ΔT; when $\Delta T \leq 0$ then the pumped energy is at its maximum, Qc_{max}. Qc reduces to zero when ΔT_{max} is reached. ΔT_{max} depends on the quality and type of the TEC.

Thermal cyclers use TECs to control the temperature of the samples in the well plate of the thermal block. The TEC's ability to pump energy allows the samples to be heated and cooled rapidly. A heat sink is used to dissipate energy and keep the temperature on the side of the TEC opposite the samples as close to ambient as possible. Typically the heat sink is force-air cooled using fans.

Thermal Energy Recovery System (TERS®)

It is desirable to maximise the heating and cooling rate in a thermal cycler in order to minimise the total time taken for an experiment. If the temperature profile required for the experiment is known or can be predicted and it is possible to control the amount of energy dissipated by the heat sink, the temperature of the heat sink can be controlled to offer an improvement in ramp rates over a system that dissipates maximum possible energy from the heat sink at all times. In a system using forced air to cool the heat sink, fan speed can be altered to affect the speed of air passing over the heat sink and hence the dissipation.

The improvement is gained by reducing the ΔT across the TEC during temperature transitions of the well plate. As the well plate is cooled, the energy from the well plate and dissipated electrical energy is pumped to the heat sink, hence its temperature rises. By dissipating very little of this energy from the heat sink by altering the speed of the fans controlling air flow over the heat sink, the temperature of the heat sink can be maintained at a desired level. The temperature the heat sink is maintained at can be chosen to minimise the ΔT across the TECs when the well plate temperature is next altered. The reduction in ΔT results in a higher Qc and hence an increase in the amount of energy pumped and conducted to the well plate giving a faster ramp rate (Figure 4).

In this way the heat sink has been used as energy store as well as a dissipater. The same improvement in ramp rates can be achieved wherever a TEC is installed in a similar system and required temperature changes are known or can be predicted.

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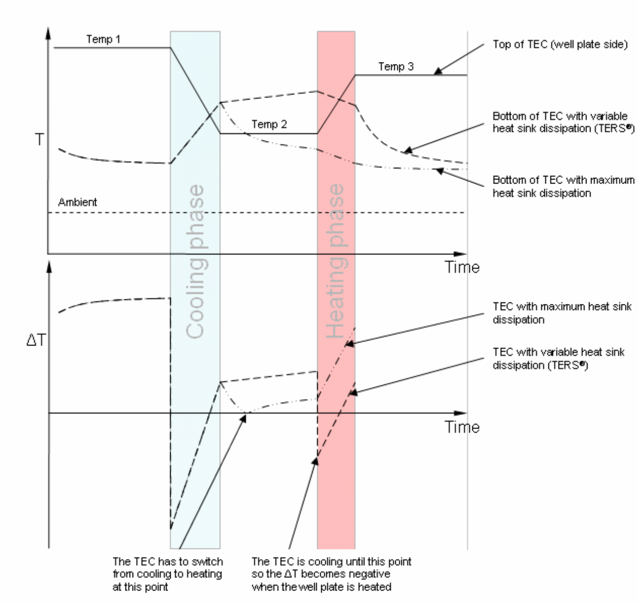

Figure 4: A sketch illustrating how the varying heat sink energy dissipation can reduce ΔT and increase ramp rates. After the cooling phase, the fans are slowed or stopped to hold the heat sink at an elevated temperature. During the heating phase, the ΔT of the TEC with variable heat sink dissipation is much lower than that with maximum heat sink dissipation resulting in a higher Qc and a faster ramping rate.

Additional Advantages of TERS®

Due to the fact that a portion of the heat energy is conserved in the heat sink and not dissipated by the fans and also because the fans are turned off for short periods of time during each cycle, it can be surmised that this would amount to a significant energy saving in the running of the thermal cycler. This was tested by running the TC-PLUS through typical 3-step and 2-step PCR protocols and measuring the energy consumed per run (Figure 5). It was found for a typical 3-step program almost 15% less energy was required with variable heat dissipation activated and around 9% less for a 2-step protocol. This would amount to considerable cost savings over the life of the thermal cycler, especially during heavy use.

Conclusions

The TERS® system offers a number of advantages for the TC-PLUS user including time-saving rapid ramp rates, the lower initial cost of the aluminium block compared to silver blocks required for other similar rapid ramping systems, plus the overall energy saved during a run. In addition, optimising reactions with specialised reagents for fast PCR protocols would also lead to shorter run times, increased throughput and lower energy costs.

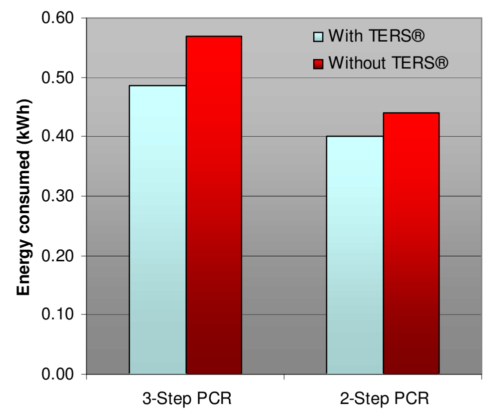

Figure 5: Energy consumed by the TC-PLUS during a thermal cycling protocol. Typical 3-step and 2-step PCR programs were run on the same unit with and without the TERS® function activated. Each program was run three times and the energy consumption measured using a plug-in power and energy monitor. The average energy consumptions for the three runs are shown.

References

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2. Hilscher, C, Vahrson, W & Dittmer, D P. Faster quantitative real-time PCR protocols may lose sensitivity and show increased variability. Nucl. Acids Res. 2005; 33(21): e182.

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