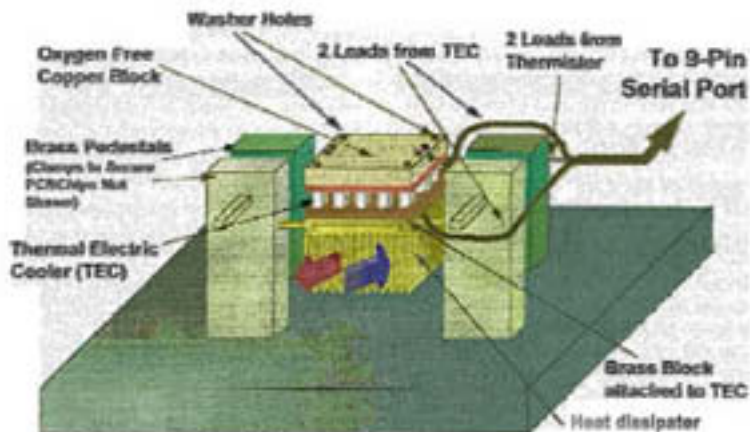


## Basic setup

A final decision on temperature control concerned the basic setup of the system; that is, which components (sensors, circuitry, etc.) to use and in what hierarchical order they should be arranged. The standard approach in the literature is summarized in Figure 70, which illustrates the basic scheme used by *Shoffner's* team in their work on PCR-chips [Cheng1996b], although there have been substantial variations on this basic design ([Wilding1994], [Taylor1997], [Lin2000a]).

In *Shoffner's* scheme, temperature is directly controlled by a commercial Peltier cell controller, which is in turn remotely controlled via RS232 by a PC programmed under Labview (*National Instruments*). The Peltier cell is located on a dissipater and bonded to an oxygen-free copper block into which a 10 k $\Omega$  thermistor has been fused. The PCR-chips are then positioned onto the copper block and held into place by clamps mounted on custom designed brass pedestals. The chips are clamped so that outlets fit tightly with machined holes in the copper block that contain rubber washers to provide adequate sealing.



**Figure 70** - False-colored image of *Shoffner's* team basic design for a Peltier (thermal-electric cooler - TEC) driven PCR-chip thermocycler.

In this research, the approach of *Shoffner's* team was used as a general guideline, although alternative layouts were assayed concerning, for example, capping strategies (see p.181). Hence, on average, the above-depicted setup was also the basic setup in the experiments described herein, even though some differences were introduced. For reasons

previously stated, custom devised circuitry substituted here the commercial temperature controller and the thermistor was also replaced by different kinds of temperature sensors (thermocouples and platinum resistors [Pt100]) placed on the Peltier surface (instead of fused within the copper block) to provide quicker reaction times and more accurate readings (see p.170-177). The RS232 connection was also replaced by a dedicated data acquisition card connection to improve precision and response times. Although temperature control could be also wired into hardware devices, this issue (together with the overall cycling control) was left to Labview programmed software in order to provide the necessary flexibility required to deal with the unforeseen problems that might arise in the accurate control of such a low thermal mass system.

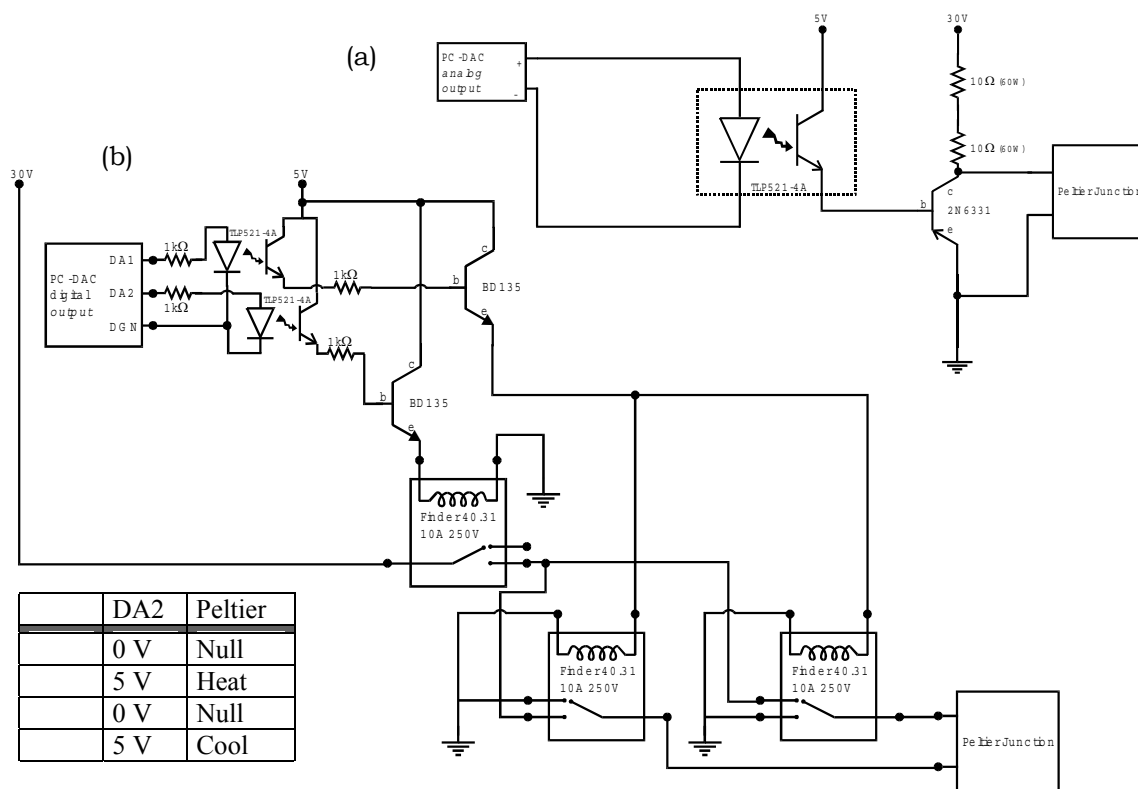
#### **4.4.4. CONTROL CIRCUITRY AND ELEMENTS**

This section covers the design of the necessary control circuitry (power driver, signal conditioning and acquisition) and the functional characterization of the necessary elements (temperature sensors and Peltier cells). The control algorithm, a proportional-integrative-derivative (PID) method, that was finally implemented will be mainly assumed as default in the following discussion and is to be further explained in a later section (see p.163).

##### **Power driver**

##### ***ON-OFF control circuitry***

Temperature control can be achieved in a number of ways, the simplest one being ON-OFF control: turning on the heater/cooler until reaching the desired temperature and turning it off after it has been reached. Notwithstanding its simplicity, ON-OFF control is routinely used in many applications (by almost all domestic thermostats) and it was the first tentative approach towards Peltier cell control in this work. After some initial implementations of ON-OFF control with transistor-based circuitries (see Figure 71a), it was observed that transistors imposed an excessive power drain on the Peltier cell, which has a relatively small non-linear resistance (around 3-5  $\Omega$ , see *Materials and Methods*, p.308), and thus limited the operation range and transitional power of the system.



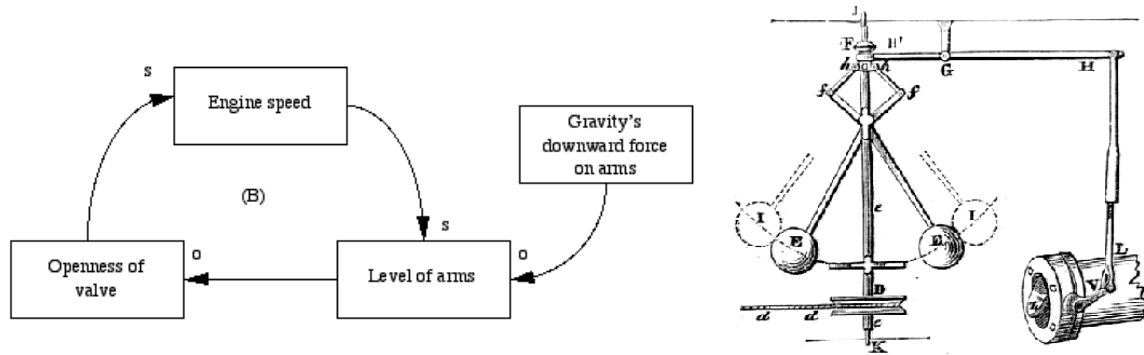
**Figure 71** - Transistor-based (a) and relay-based (b) schematics. In both cases a digital opto-coupler is used to electrically isolate the power system from the data acquisition board (DAC). The transistor-based scheme is a heating-only ON-OFF system, while the relay-based scheme is a dual heater/cooler ON-OFF system (see logic table at left).

To avoid this problem, a relay-based circuitry was implemented (see Figure 71b), but the experimental results (data not shown, see Figure 78) evidenced that accurate ( $\pm 1\text{ }^{\circ}\text{C}$ ) temperature control with an ON-OFF system was not possible within the proposed framework, since the system had a too low thermal mass. Hence, even if ON-OFF transients were sped up, accuracy would always require lower power levels and a tradeoff would inevitably had to be paid in terms of temperature transition times. Moreover, due to their own nature (see *Materials and Methods*, p.305), Peltier cells do not withstand ON-OFF control handsomely, since electro-migration phenomena tend to degrade the PN junction that is the core of the Peltier effect and thus limit the cell's lifespan.

### **PID control circuitry**

ON-OFF control is the simplest negative-feedback control system conceivable and its simplicity comes mainly from the fact that it is a

discrete control system, with only two different states: ON and OFF. Discarding ON-OFF circuitry meant that a continuous negative-feedback system had to be implemented. The simplest among these is the proportional control, exemplified by the clever design of Watt's steam engine governor ([Webb1970], see Figure 72).

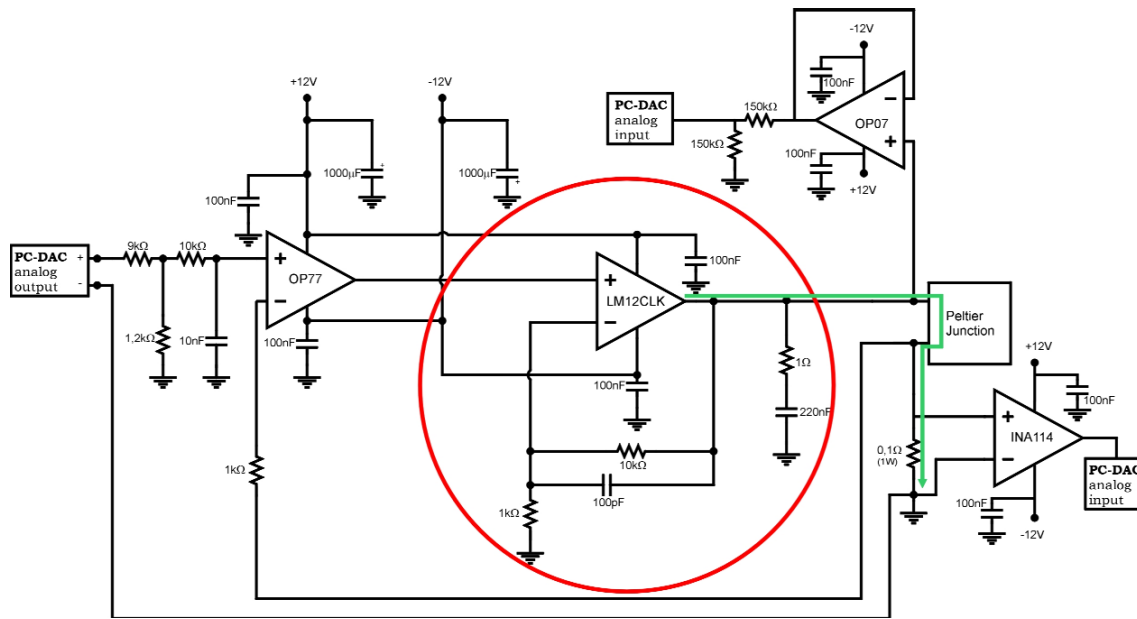


**Figure 72** - Watt's (or centrifugal) steam engine governor. A pair of balls on hinged arms spin round, driven by the engine through a pulley (D) and, in turn, regulating the engine's valve (V) by means of a geared arm (G, H). Lower speed decreases rotation and hangs down the arms (E), opening the valve. Conversely, high speeds increase rotation and raise the arms' level (I), thus closing the valve. Source: [Dawkins1989].

As it will be seen (see p.165), proportional control can be further elaborated and complicated with the introduction of derivative and integrative factors, but, in the basic setup of this work, these are items that were dealt with by software programming. Thus, in terms of the power driver circuitry, the only fact that holds true for all proportional control systems is that regulation is achieved by continuous (as opposed to discrete ON-OFF) modification of the power delivered to the actuator. Continuous (that is, functionally continuous) drive can be accomplished by different methods, such as pulse-width or voltage modulation. Due to the negative effects of pulse-based systems on Peltier cells (see p.152), it was decided to build a voltage-modulation driver.

### ***Voltage-modulation driver***

After some trials with different power operational amplifiers to best-fit Peltier cell requirements (see *Materials and Methods*, p.307), a basic driver circuitry schematic was devised and is shown in Figure 73.



**Figure 73** - Voltage-modulation, voltage-controlled driver schematic.

In this schematic, the red-circled region containing the LM12CLK 80W power op-amp (*National Semiconductor*) is the main power stage. This stage drains power from a dual  $\pm 12$  V-10 A custom-assembled FE-17 power supply (*Cebek*) and amplifies the signal voltage of the OP77 op-amp (*Analog Devices*) eleven-fold ( $1+10$  k $\Omega$ /1 k $\Omega$ ) in a non-inverter amplifier loop. The OP77 stage, in turn, acts as a driver for the power stage and is directly controlled by the data acquisition board analog output after a voltage-divider step to allow better resolution control with the 12bit analog output. The only possible current flow, due to the virtual ground assumption of operational amplifier inputs, is illustrated by the green line and can be directly calculated from the DAC output voltage with the simple formula:

$$I_{\text{Peltier}} = \frac{\left( \frac{1.5 \cdot V_{\text{DAC}}}{9 + 1.5} \right)}{0.1}$$

**Equation 2** - Current flowing through the Peltier cell in terms of DAC control voltage. The 0.1 factor corresponds to the 0.1  $\Omega$  power resistor, whilst the other term in the Ohm equation corresponds to a classic voltage divider.

The real power consumption of the Peltier cell can be checked using the output provided by the OP07 voltage follower (*Texas Instruments*) and the

INA114 precision differential amplifier (*Burr-Brown*), a fact that was later also used in the initial evaluation of polysilicon resistors (see p.228). In essence:

$$P_{Peltier} = V_{Peltier} \cdot I_{Peltier} \quad \Leftarrow \quad V_{Peltier} = V_{OP07} - V_{INA114} \quad \& \quad I_{Peltier} = \frac{V_{INA114}}{0.1}$$

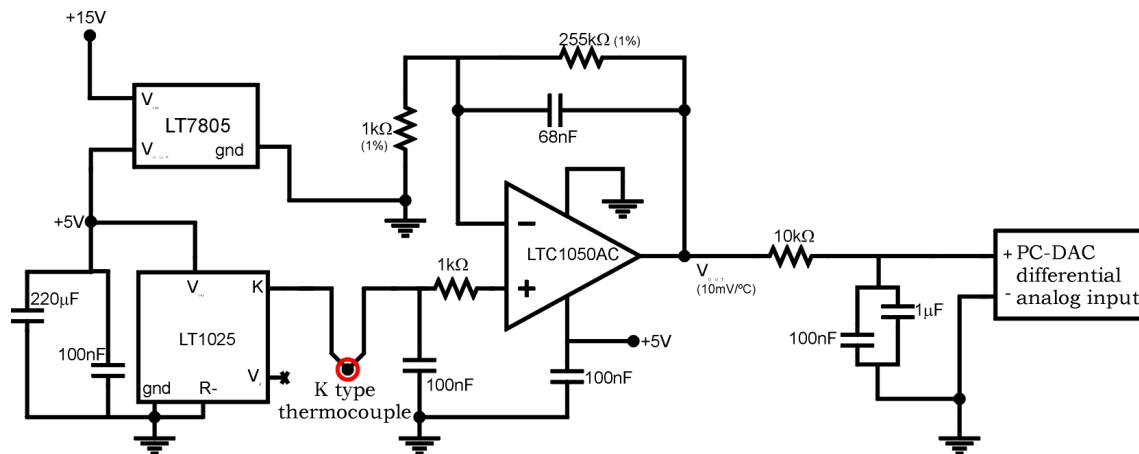
**Equation 3** - Accurate reading of the real power consumption of the Peltier cell.

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## Sensors

### Thermocouple circuitry

Thermocouples, temperature sensors based on the Seebeck effect, are typically more stable and offer better precision than thermistors. They are also best suited for surface measurements and have faster reaction times (see *Materials and Methods*, p.309). Hence, it was initially decided to use thermocouples for accurate sensing of the temperature in the custom fast thermocycler, since they provided enough accuracy ( $\sim \pm 0.5 \text{ }^\circ\text{C}$ ) and the fast transient times required for high-power, fast PID control. After some redesigns concerning the nature of the operational amplifiers used and filtering issues, the final schematic for thermocouple signal conditioning is presented in Figure 74.



**Figure 74** - Thermocouple temperature reading circuitry

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At the heart of the circuit lies a LT1025 Thermocouple Cold Junction Compensator (*Linear Technology*). Thermocouples are based on the Seebeck effect (see *Materials and Methods*, p.305), which postulates that a current flow will originate in a closed loop circuit composed of two distinct

metals or semiconductors if one of the metal-metal (or PN) junctions is at a different temperature than the other. This phenomenon can be exploited to measure temperature if the temperature at one of the junctions (the "cold" junction) is known, a fact that is typically achieved in the laboratory by immersion of the cold junction in an icy water bath ( $\sim 0\text{ }^{\circ}\text{C}$ ). In this case, the current flowing across the thermocouple will give a reliable measure of the temperature at the "hot" junction. Alternatively, temperature can be measured at the cold junction (with, for instance, a thermistor) and the hot junction temperature can be obtained by simply adding the thermistor-read temperature to the thermocouple "hot" junction read temperature.

The LT1025 and other cold junction compensators have an integrated temperature sensor that reads the cold junction temperature (assumed to be that of the board onto which the chip is mounted). With these readings, compensators do then inject current into the loop to compensate for the non-zero  $^{\circ}\text{C}$  temperature of the cold junction. In the above schematic, the compensated current for a K-type thermocouple is then read by a low-noise LT1050 op-amp (*Linear Technology*) and amplified 256-fold in a non-inverter amplifier loop (yielding, approximately,  $10\text{ mV}/^{\circ}\text{C}$  values). Due to the necessity of providing accurate results, a LT7805 (*Linear Technology*) was inserted to provide a stable 5 V voltage supply from a standard laboratory FAC-6628  $\pm 15\text{ V}$ -1 A dual power supply (*Promax*), and C and RC filter stages were introduced in amplifying loops and at the output. Thermocouple readings were then software-adjusted using a look-up-table to interpolate the non-linear behavior of K-type thermocouples (see *Materials and Methods*, p.312), based on experimental calibration in water with reference thermometers (see *Materials and Methods*, p.310).

### ***Platinum resistance circuitry***

After some unsuccessful experiments on PCR amplification with passive chips, and as a safety measure to guarantee that temperature control could not be the culprit, it was decided to switch to more precise temperature sensors. Platinum resistive thermal devices (PRTD) are the most precise surface temperature sensors available, displaying accuracies of down to  $\pm 0.01\text{ }^{\circ}\text{C}$ . With the aim of maximally reducing possible temperature accuracy problems, a 4-wire class-A 1/10-DIN Pt100 RTD (*Kosmon*), capable of providing  $\pm 0.01\text{ }^{\circ}\text{C}$ , was acquired and a specialized circuitry (see Figure 75) was devised to operate it.