PCR Biochip

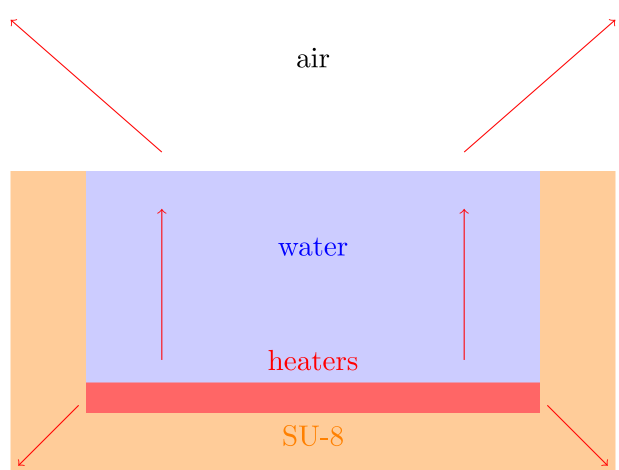
In this problem, we will develop an analogy to simplify the analysis of heat transfer in materials which can greatly help in getting some heuristic estimates for complicated problems of interest. In particular, in this problem we will estimate the length scale required to build a "PCR biochip" – a device which can induce the polymerase chain reaction (PCR), which is used to create a huge number of identical strands of DNA given only a few to start with. This reaction has proved to be one of the most important developments for modern experimental biology.

In order to be most effective, PCR must be performed in an environment which is switching between temperatures of roughly 55, 75 and 95°C. The key question we have to ask is what devices can transition between these temperatures, and uniformly heat the water in which PCR occurs, on the order of < 1 s, in order to have fast reactions.

Before we begin modeling the PCR biochip, let us take a detour and describe the simplification we will use to model this problem. Our goal is to model the complicated flow of heat throughout the materials making up the chip by simplifying the problem and reducing it to an RC-circuit problem. We can then use our knowledge of how to solve circuit problems to estimate the time scale over which the thermal system will relax to thermal equilibrium. So to begin with, suppose that we have a block of some material, which has a temperature difference $\theta = T_{\text{top}} - T_{\text{bottom}}$ between its top and bottom, which are separated by a distance h. Assume that the cross section of the material is A.

(a) Show that if I is the heat flux through the block of material, that $\theta = IR$, and find an expression for the thermal resistance R in terms of A, h, and the thermal conductivity κ.

(b) Show that the body also acts as a capacitor: if Q is the total heat absorbed by the material as it heats up an amount ΔT, show that $Q = C\theta$, and find an expression for C in terms of the specific heat per volume c, and A and h.

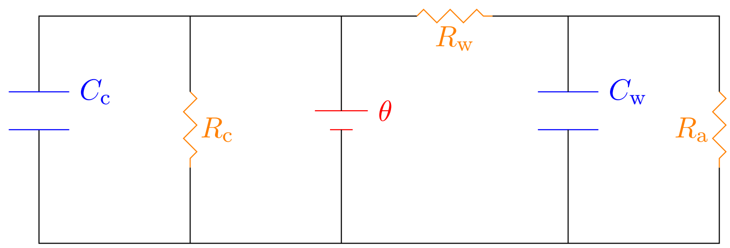


Now, let us describe the simplest possible model for the PCR biochip, as shown in the figure above. We have a body of water containing the DNA and polymerase proteins surrounded by a container built with a polymeric material called SU-8. Heaters placed at the bottom of the water heat the water, as well as the SU-8. Heat flow also escapes to the air above the container. Due to the complicated nature of convection, and the infinite height of the air, it turns out that the appropriate model for the thermal resistance R is simply

$$R_{\mathrm{a}} = \frac{1}{KA}$$

where A is the area of the water-air surface, and K is a heat transfer coefficient for convection. In the figure above, the red arrows crudely depict the flow of heat. If the ambient temperature is T_0, the heaters are raised to a temperature $T_0 + \theta_0$. Finally, for the remainder of this problem, you may set all surface areas $A = L^2$, and all heights $h = L$, where L is the characteristic length scale of the problem. Our goal will be to determine the requirements on L so that the biochip works effectively.

(c) Argue that the following is a reasonable "circuit approximation" for the PCR biochip:



Here R_{c} and C_{c} are the thermal resistance/capacitance of the SU-8 container, R_{w}, C_{w} are for the water, and R_{a} is for the air. Why do we not need to worry about adding a capacitor for air?

(d) Determine the time scale over which the water bath will reach thermal equilibrium. What are the constraints on L, given that this time scale should be much smaller than 1 s?

(e) Estimate the temperature of the water, in "thermal equilibrium", in steady-state, as a function of L. Is the requirement that the temperature of the water be close to $T_0 + \theta_0$ a limiting constraint in the design of the biochip?

(f) How much power does it cost to maintain the heaters at a temperature by $\theta = 50$ K above ambient temperature, in steady-state? To answer this question, plug in a value for L which satisfies the design constraints outlined in the previous two parts.

Only since 2000 or so has it been possible to build biochips on the very small length scales that you should have found in this problem.

For this problem, you may find the following data useful. This data is for temperatures of order 300 K, which are appropriate for this problem. The "heat transfer coefficient" K for air is $K \approx 7.5$ W/m$^2 \cdot$K. For water and SU-8 we have the following data:

material	κ (W/m $\cdot$ K)	c (kJ/m^3)
water	0.60	4200
SU-8	0.20	1800