CMP 610b Lecture 2
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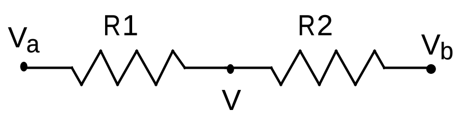
Amplifiers and Feedback

In this lecture we consider some basic principles of electronics that are important for understanding how voltage clamps and patch clamps work.

VOLTAGE DIVIDERS

We first consider the properties of two resistances in series. These could be resistances like the resistance of a microelectrode or of a cell membrane, or the electronic components called resistors, which consist of an insulating cylinder on which a thin metal film is deposited to make a device with a known resistance. Suppose two resistances are arranged like



What is the voltage V in the center, if V_a and V_b are imposed on the ends? One way to solve this is to notice that the current flowing through the resistors will be the voltage difference at the ends, divided by the total reisistance,

$$I = \frac{V_a - V_b}{R_1 + R_2}$$

so, working from the left-hand end we have

$$V = V_a - IR_1$$

which after some algebra works out to

$$V = \frac{V_a R_2 + V_b R_1}{R_1 + R_2} \qquad (1)$$

i.e. a weighted average of the voltages at the ends. This is just like the result we had last time, where we had a voltage V imposed on a microelectrode and the resting potential of a cell acting through the cell's membrane resistance, which happend to be equal to the electrode resistance; the result was a potential halfway between.

OPERATIONAL AMPLIFIERS

The key components in things like voltage clamps are little integrated circuits called operational amplifiers. They have five useful terminals coming out of them. Two of them connect to power supplies (typically +15 and –15 volts); two are inputs and one is an output terminal. We make a diagram of one like this (ignoring the power supply terminals which of course have to be hooked up for things to work),

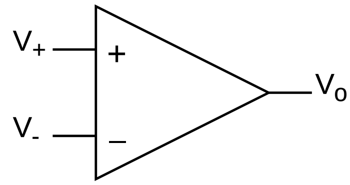


Fig. 1

Here V_+ and V_- are the voltages on the non-inverting and inverting inputs, respectively, and V_o is the output voltage. A simple description of an operational amplifier is provided by the following equations.

$$i_+ = 0$$

$$i_- = 0$$

$$\frac{dV_o}{dt} = \alpha\,(V_+ - V_-). \qquad (2)$$

The first two equations say that no current flows into the two input terminals; the amplifer measures voltages without taking any current (this is not strictly true, but is usually a good approximation!). The third equation says that if any voltage difference exists between the input terminals, the output voltage starts to change. The constant α is usually a large number, on the order of 10^7/second. Thus even a small difference causes a rapid change in V_o.

INVERTING AMPLIFIERS

We will now hook up this operational amplifier in ways to make various sorts of useful devices. First let us use it with two resistors like this:

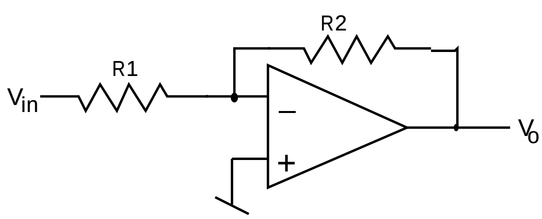


Fig. 2

We have connected the non-inverting input to 'ground' (i.e. the point where we say the potential is zero), apply an input signal V_{in} through R_1 and have connected R_2 as a 'feedback' resistor, because it connects the output back to the input. We can use equation (1) to compute what V_o is, given what V_{in} is.

$$\frac{dV_o}{dt} = -\alpha\,\frac{V_{in}R_2 + V_oR_1}{R_1 + R_2}$$

which can be rearranged to a standard form

$$\left(\frac{R_1+R_2}{\alpha R_1}\right)\frac{dV_o}{dt} + V_o = -\frac{R_2}{R_1}\,V_{in} \qquad (3)$$

The term $(R_1+R_2)/(\alpha R_1)$ is the time constant, and $-(R_2/R_1)V_{in}$ is the final value, of the response of this circuit to a sudden change in V_{in}. For example if $R_1 = R_2$ then V_o will follow V_{in}, only it will be inverted and it will be delayed slightly by a time constant of $2/\alpha$, something on the order of 0.1µs. If we made the ratio R_2/R_1 quite large, say by making $R_2 = 10^6\Omega$ and $R_1 = 10^3\Omega$ then we would have an amplifier with a 'gain' of –1000. The time constant would be roughly $1000/\alpha$, or about 100µs.

CURRENT TO VOLTAGE CONVERTER

Here is another way of thinking about the amplifiers we just discussed. Because of the feedback connection via R_2, the amplifier always acts to keep the voltage at its inverting input at zero. Transiently it will be nonzero when a sudden change is made, but it will return to zero with a short time constant. So we say that the inverting input is approximately at zero.

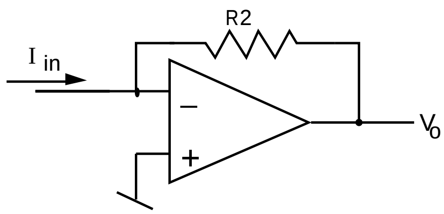


Fig. 3

Then if we inject a current I_{in} at the input, this current must be flowing through R_2 (since no current flows into the amplifier inputs). For V_- to be zero, we must then have

$$V_o \approx -I_{in}R_2 \qquad (4)$$

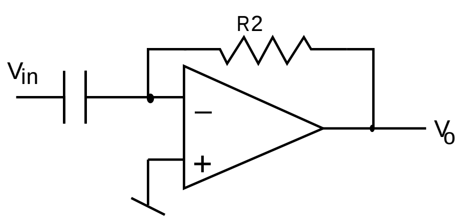
Suppose I_{in} is created by a voltage applied through a resistor R_1 (as in Fig. 2). Then $I_{in} \approx V_{in}/R_1$ and the final relationship is

$$V_o \approx -V_{in}\,(R_1/R_2)$$

This is a restatement of eqn. (3), only where we have ignored the time dependence.

There are two interesting things to note about the circuit of Fig. 3 and its eqn. (4).

1. It does not matter how I_{in} is created, the output voltage will always be proportional to it. Thus we can make amplifiers that sum multiple inputs by connecting multiple inputs through resistors to the inverting input of the amplifier.
2. You can connect things other than resistors to the input. For example, suppose you connect a capacitor:

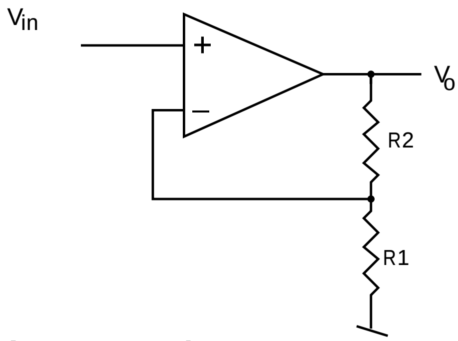


Since I_{in} will equal $C(\frac{dV_{in}}{dt})$ this will act as a differentiator, with

$$V_o \approx -R_2 C(\frac{dV_{in}}{dt}).$$

NON-INVERTING AMPLIFIERS

We consider one more amplifier configuration. This is one where V_o has the same sign as V_{in}. It is made the following way:



The output voltage is given by

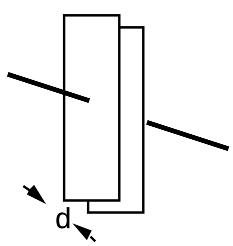
$$V_o \approx \frac{R_1+R_2}{R_1} V_{in}. \tag{5}$$

You can convince yourself that this is true by remembering first that V_o changes whenever V_- and V_+ are unequal, so the negative feedback will tend to keep them equal; and, second, making use of the voltage divider formula (eqn. 1).

CAPACITANCE IN MICROELECTRODES

Now let me return to a topic I did not cover last time. We considered the problem of trying to control the membrane potential of a cell with a microelectrode. Now we consider the problem of measuring a potential with a microelectrode. The problem has to do with the electrode resistance and its capacitance.

Capacitance is the ratio of the amount of stored charge at an interface to the applied potential difference. For a capacitor made of two metal plates (or made of other conducting surfaces)



the capacitance is

$$C = \frac{A}{d} \varepsilon_0 \varepsilon$$

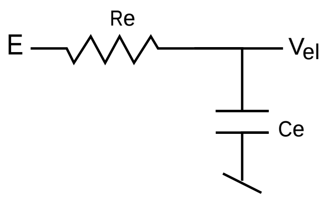
Here A is the area of each plate, d is the spacing, ε_0 is a physical constant that is about equal to

10^{-13} farads per cm (i.e. 0.1 pF / cm), and ε is the dielectric constant, a property of the material between the plates.

Now consider a microelectrode immersed in a bath solution. The pipette is pulled from a glass capillary with diameter ~1mm and wall thickness ~0.1 mm. As the capillary is pulled the diameter and the wall thickness decrease proportionately. Therefore you can convince yourself that the capacitance, per unit length of the pipette, between the conducting solution inside the pipette and the solution outside does not vary as the pipette tapers down to a narrow tip. The ratio A/d will be constant, in our case, as

$$\frac{A}{d} = \frac{\pi \times 1\text{mm} \times l}{0.1\text{mm}}$$

for a length l. The total capacitance works out (with $\varepsilon \approx 3$) to be about 10 pF per cm of pipette length. Is this a serious amount of capacitance? Remember last time that the resistance in a pipette is concentrated at the tip. A good electrical model for a pipette that is sensing a voltage E is therefore



where we have 'lumped' all of the electrode resistance at the tip, and place most of the capacitance of the electrode at the other end.

We can write an equation for how the measured voltage V_{el} compares to the actual voltage E. The equation is

$$R_e C_e \frac{dV_{el}}{dt} + V_{el} = E.$$

This says that the response to a step change in E will be an exponential relaxation in V_{el}, with time constant $\tau = R_e C_e$. A high-resistance electrode can have a resistance of 100 MΩ or more. If C_e is 1 pF this results in a time constant of 100μs or more. Usually the electrode holder and the amplifier contribute some more capacitance, perhaps several more picofarads, so that the time constant can be relatively large.