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Directions for homework submission

Submit each of your homework to canvas as the pdf output of the jupyter notebook, and a zip of the jupyter notebook (.ipynb), and all other necessary attachments (e.g. images). Name your files starting in the format of "Last_name_First_name_File_name" separated by underscores.

For example, Jieyu submits two files for her homework this week:

1. Zheng_Jieyu_HW1.pdf (the pdf output of the jupyter notebook)

   If you have problems rendering your notebook into pdf, you can open your notebook in a browser and print -> save as pdf.
2. Zheng_Jieyu_HW1.ipynb

Please make sure your notebook can be run without errors within the cns187 virtual environment. Any file that fails to be executed on TA's end will be considered as late submissions.

Caltech Honor code: Searching for the solutions online is strictly prohibited. You should refer to the textbooks and lecture slides. If you are citing any external sources online, please include a list of references.

Collaboration on homework assignments is encouraged. However, **you cannot show each other the numerical answers or codes**. Please note at the beginning of each answer whom you have discussed the problems with (including TAs).

All the mathematics should be typed in Latex format. You may work on a piece of paper and then type it into the notebook. Here is a useful [cheat sheet (http://users.dickinson.edu/~richesod/latex/latexcheatsheet.pdf)](http://users.dickinson.edu/~richesod/latex/latexcheatsheet.pdf). Please do not submit pictures of handwritten maths.

For the schematic and drawings to be submitted, please display the images in markdown cells in your homework amd make sure they show up in your pdf rendering.

Please make sure that all your plots include a title and axis labels with units. One point will be deducted for each missing element.

Environment configuration in terminal

You should have already completed these steps if you followed the instructions on Canvas. Let us know if you have any questions in the process.

1. Install conda on your operating system.
2. Create a new environment for this course by running the following commands:

```
conda create -n cns187 python=3.7
conda activate cns187
# Under the new environment install the following packages
conda install pip numpy scipy matplotlib pytest ipython no
tebook
```

Simulation package

3. Install [Nengo (https://www.nengo.ai/)](https://www.nengo.ai/), a simulation package via pip install:

```
pip install nengo nengo-gui
```

Check if the installation is successful by typing in the cns187 environment:

```
nengo
```

A browser screen should come up with code and GUI pannels.

We will start using it in the next one. If you encounter any installation issues, please come to the TA office hour for help.

Optional packages

Your code should follow the PEP 8 guidelines. We also recommend code formatting tools such as black (https://github.com/psf/black); a useful extension is blackcellmagic (https://github.com/csurfer/blackcellmagic). You can install the extension with the following code (this is optional):

```
conda install black
pip install blackcellmagic
```

You may also install jupyter notebook extensions (https://jupyter-contrib-nbextensions.readthedocs.io/en/latest/install.html) for your convenience.

In general, we hope that everyone uses the same packages for their homework. We will update you at the beginning of each homework if more packages are needed. If you recommend any additional packages, please talk to the TAs!

Order of Magnitude Neuroscience (25 pts)

Membrane Capacitance (15 pts)

The textbook value for a neuronal membrane capacitance is $1\mu\mathrm{F/cm}^2$. Convince yourself that this is reasonable.

Hints:

1. Treat the lipid bilayer membrane like a parallel plate capacitor with a dielectric between the plates
2. Assume that the electrolyte on both sides of the membrane is a perfect conductor

Phospholipid bilayer membrane thickness: $d \approx 3 - 5nm$

Phospholipid bilayer membrane dielectric constant: $\kappa \approx 5$

Capacitance formula: $\kappa \cdot \frac{\epsilon_0 \cdot A}{d}$

Neuronal membrane capacitance: $5 \cdot \frac{8.854 \times 10^{-12} F \cdot m^{-1}}{4 \times 10^{-9} m} \approx 0.0110675 \frac{F}{m^2} = 1.10675 \frac{\mu F}{cm^2}$

This matches very closely the textbook value for a neuronal membrane capacitance.

Sensitivity of the senses (10 pts)

Which is more sensitive: vision or touch? The answer is obvious, but by how much? Humans can see single photons. What is the weakest touch stimulus? The palm of your hand is a pretty sensitive area. Try dropping a rice grain on it, can you feel that? From what height? What about a grain of sand? Once you've measured the weakest touch stimulus you can feel, compare its energy to that of a photon. **How many orders of magnitude difference?**

Hint:

- Check [this wikipedia (https://en.wikipedia.org/wiki/Photon_energy)](https://en.wikipedia.org/wiki/Photon_energy) for how to calculate photon energy of visible light
- Check [this wikipedia (https://en.wikipedia.org/wiki/Gravitational_energy)](https://en.wikipedia.org/wiki/Gravitational_energy) for how to calculate gravitational energy.

Since we are obviously close to earth's surface the gravitational energy can be calculated using $U = mgh$

Mass of a grain of sand: $\approx 0.00001562g$

Distance of drop: $\approx 1mm$

$g \approx 9.8m/s^2$

$$U = 1.562 \times 10^{-8}g \cdot 9.8m/s^2 \cdot 1 \times 10^{-3}m = 1.53076 \times 10^{-10}J$$

For the photon energy of visible light we use $E = \frac{hc}{\lambda}$

$c \approx 3 \times 10^8$

$h \approx 6.626 \times 10^{-34}m^2kg/s$

Wavelength of visible light: $380 - 700nm$

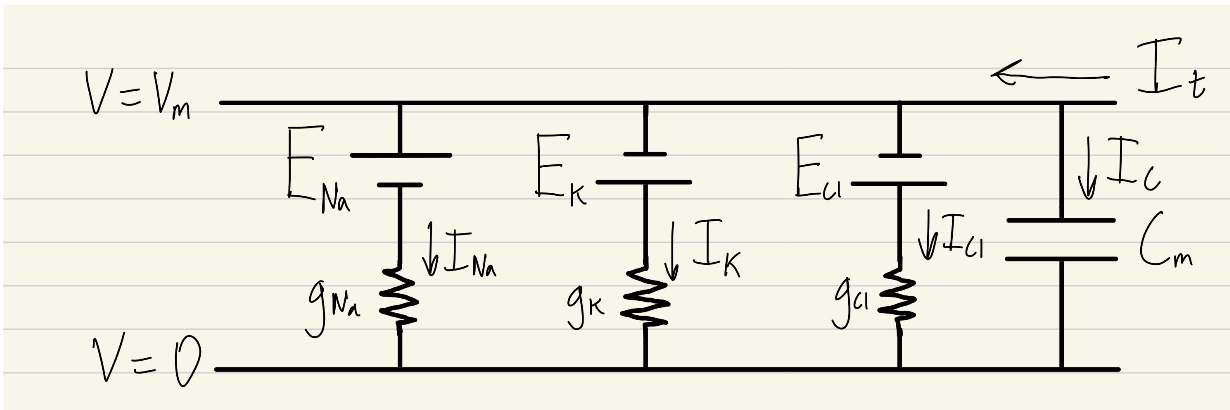
$E \approx 2.83 \times 10^{-19} - 5.23105 \times 10^{-19}$

The order of magnitude difference is ≈ 10

Equivalent circuit and resting membrane potential (35 pts)

Equivalent circuit (10 pts)

Draw an equivalent circuit model for a neuronal cell membrane that is permeable to Na^+, K^+, AND Cl^-. Be sure to include the capacitive current! From the circuit model, derive a differential equation for the transmembrane potential V_m. Explain the meaning of each term in this equation and what physical properties determine it.



$$I_c + I_{Na} + I_K + I_C l = I_t$$

$Q_{C_m} = C_m \cdot V_m$

$I_c = \frac{dQ}{dt} = C_m \cdot \frac{dV_m}{dt}$

$V = IR \implies I = \frac{V}{R} = g \cdot V$

$$C_m \cdot \frac{dV_m}{dt} + g_{Na} \cdot (V_m - E_{Na}) + g_K \cdot (V_m - E_K) + g_{Cl} \cdot (V_m - E_{Cl}) = I_t$$

$$C_m \cdot \frac{dV_m}{dt} + V_m \cdot (g_{Na} + g_K + g_{Cl}) = I_t + g_{Na}E_{Na} + g_K E_K + g_{Cl} E_{Cl}$$

The equation shows us that the change in voltage is dependent on the conductances of Na^+, K^+, AND Cl^- as well as the capacitive current. One can also see that settin I to 0 and V to 0 gives the standard formula for resting potential. Additionally currents form due to the Nernst potentials and conductances of the molecules as they permeate as seen on the right hand side of the differential equation above.

Crater Lake Crabs (25 pts)

You examine a new species of freshwater crab living in Crater Lake in Oregon, and to your surprise, you find that the resting membrane potential of neurons in the gut of these animals is determined by Cs^{+} and Mg^{2+} ions.

The intracellular and extracellular concentration of Cs^{+} and Mg^{2+} ions in these crabs are as follows:

$[\mathrm{Cs}]_\mathrm{e} = 10\mathrm{mM},$

$[\mathrm{Cs}]_\mathrm{i} = 150\mathrm{mM},$

$[\mathrm{Mg}]_\mathrm{e} = 1\mathrm{mM},$

$[\mathrm{Mg}]_\mathrm{i} = 0.01\mathrm{mM}.$

The conductance of g_{Cs} is 4 nS, and that of g_{Mg} is 1 nS.

a) Calculate the equilibrium potential, E_{Cs} and E_{Mg}, at 5 $^{\circ}\mathrm{C}$ using the Nernst equation.

$e = 1.6 \times 10^{-19} C \quad k = 1.381 \times 10^{-23} \frac{J}{K}$

$5^{\circ} = 278.15K$

$g_{Cs} = 4ns \quad g_{Mg} = 1nS$

$z_{Cs} = 1 \quad z_{Mg} = 2$

$$E_{Cs} = -\frac{kT}{z_{Cs} \cdot e} \cdot \ln \frac{[Cs]_i}{[Cs]_e} = -0.06501438686V \approx -65.01mV$$

$$E_{Mg} = -\frac{kT}{z_{Mg} \cdot e} \cdot \ln \frac{[Mg]_i}{[Mg]_e} = 0.05528005276V \approx 55.28mV$$

b) Calculate the resting potential, V_{rest}, for this surprising species.

$$V_{rest} = \frac{g_{Cs} \cdot E_{Cs} + g_{Mg} \cdot E_{Mg}}{g_{Cs} + g_{Mg}} = -0.04095549893V \approx -40.96mV$$

Dynamics of dendritic conduction (40 pts)

In W1L1, we learned about the cable equation for passive conduction along a leaky cable:

$$\lambda^2 \frac{\partial^2 V}{\partial x^2} = \tau \frac{\partial V}{\partial t} + V$$

We discussed the steady-state solution: If $\frac{\partial V}{\partial t}$ = 0, then the equation is solved by

$$V(x) = V_0 \, \mathrm{e}^{\pm \mathrm{x}/\lambda}$$

with the exponent of either sign.

For example, if the cable extends infinitely from $x = -\infty$ to $x = +\infty$, and we apply a voltage V_0 at $x = 0$ then the appropriate solution is

$$V(x) = V_0 \, \mathrm{e}^{-|\mathrm{x}|/\lambda}$$

so the voltage decays exponentially in both directions from $x = 0$.

Now we would like to know the full time-dependent solution. In particular, suppose the voltage at $t = 0$ is a brief pulse that injects some charge into the cable. How does that voltage pulse propagate down the cable?

Analytical solution (10 pts)

Show that

$$V(x,t) = \frac{1}{\sqrt{4\pi t/\tau}} \exp\left(-\frac{\tau x^2}{4\lambda^2 t}\right) \exp\left(-\frac{t}{\tau}\right)$$

satisfies the cable equation. This is called the Green's function for the problem.

$$V(x,t) = \frac{1}{\sqrt{4\pi t/\tau}} \exp\left(-\frac{\tau x^2}{4\lambda^2 t}\right) \exp\left(-\frac{t}{\tau}\right) = \frac{\exp\left(-\frac{\tau x^2}{4\lambda^2 t} - \frac{t}{\tau}\right)}{2 \cdot \sqrt{\pi t/\tau}} = \frac{\sqrt{t} \cdot \exp\left(-\left(\frac{\tau x^2}{4\lambda^2 t}\right.\right.}{2t \cdot \sqrt{\pi/\tau}}$$

1 - Calculating derivative with respect to t:

$$(1.1) \quad \frac{\partial V}{\partial t} = \frac{1}{2\sqrt{\pi/\tau}} \cdot \frac{\partial}{\partial t}\left(\frac{\exp\left(-\frac{\tau x^2}{4\lambda^2 t} - \frac{t}{\tau}\right)}{\sqrt{t}}\right)$$

$$(1.2)\quad \frac{\partial V}{\partial t} = \frac{1}{2\sqrt{\pi/\tau}} \cdot \frac{-\sqrt{t}\,\left(-\frac{\tau x^2}{4\lambda^2 t^2} + \frac{1}{\tau}\right)\exp\left(-\left(\frac{\tau x^2}{4\lambda^2 t} + \frac{t}{\tau}\right)\right) - \frac{1}{2\sqrt{t}}\exp\left(-\left(\frac{\tau x^2}{4\lambda^2 t}\right.\right.}{t}$$

$$(1.3)\quad \frac{\partial V}{\partial t} = \frac{1}{2\sqrt{\pi/\tau}} \cdot \frac{\left(\sqrt{t}\,\left(\frac{\tau x^2}{4\lambda^2 t^2} - \frac{1}{\tau}\right) - \frac{1}{2\sqrt{t}}\right)\exp\left(-\left(\frac{\tau x^2}{4\lambda^2 t} + \frac{t}{\tau}\right)\right)}{t}$$

$$(1.4)\quad \frac{\partial V}{\partial t} = \frac{\left(\frac{\tau x^2}{4\lambda^2 t^{3/2}} - \frac{\sqrt{t}}{\tau} - \frac{1}{2\sqrt{t}}\right)\cdot\exp\left(-\left(\frac{\tau x^2}{4\lambda^2 t} + \frac{t}{\tau}\right)\right)}{2t\sqrt{\pi/\tau}}$$

2 - Calculating derivative with respect to t multiplied by tau:

$$(2.1)\quad \tau\frac{\partial V}{\partial t} = \frac{\left(\frac{\tau^2 x^2}{4\lambda^2 t^{3/2}} - \sqrt{t} - \frac{\tau}{2\sqrt{t}}\right)\cdot\exp\left(-\left(\frac{\tau x^2}{4\lambda^2 t} + \frac{t}{\tau}\right)\right)}{2t\sqrt{\pi/\tau}}$$

$$(2.2)\quad \tau\frac{\partial V}{\partial t} + V = \frac{\left(\frac{\tau^2 x^2}{4\lambda^2 t^{3/2}} - \sqrt{t} - \frac{\tau}{2\sqrt{t}}\right)\cdot\exp\left(-\left(\frac{\tau x^2}{4\lambda^2 t} + \frac{t}{\tau}\right)\right)}{2t\sqrt{\pi/\tau}} + \frac{\sqrt{t}\cdot\exp\left(-\left(\frac{\tau}{4.}\right.\right.}{2t\sqrt{\pi/}}$$

$$(2.3)\quad \tau\frac{\partial V}{\partial t} + V = \frac{\exp\left(-\left(\frac{\tau x^2}{4\lambda^2 t} + \frac{t}{\tau}\right)\right)\cdot\left(\frac{\tau^2 x^2}{4\lambda^2 t^{3/2}} - \frac{\tau}{2\sqrt{t}}\right)}{2t\sqrt{\pi/\tau}}$$

3 - Calculating second derivative with respect to x:

$$(3.1)\quad \frac{\partial V}{\partial x} = \frac{1}{\sqrt{4\pi t/\tau}}\cdot\exp\left(-\frac{t}{\tau}\right)\cdot -\frac{2\tau x}{4\lambda^2 t}\cdot\exp\left(-\frac{\tau x^2}{4\lambda^2 t}\right)$$

$$(3.2)\quad \frac{\partial^2 V}{\partial x^2} = \frac{1}{\sqrt{4\pi t/\tau}}\cdot\exp\left(-\frac{t}{\tau}\right)\cdot\left(\frac{4\tau^2 x^2}{16\lambda^2 t^2}\cdot\exp\left(-\frac{\tau x^2}{4\lambda^2 t}\right) - \frac{2\tau}{4\lambda^2 t}\cdot\exp\left(-\frac{\tau}{4.}\right.\right.$$

$$(3.3)\quad \frac{\partial^2 V}{\partial x^2} = \frac{\exp\left(-\left(\frac{\tau x^2}{4\lambda^2 t} + \frac{t}{\tau}\right)\right)\cdot\left(\frac{\tau^2 x^2}{4\lambda^4 t^2} - \frac{\tau}{2\lambda^2 t}\right)}{2\sqrt{\pi t/\tau}}$$

$$\frac{\partial^2 V}{\partial x^2} = \frac{\exp\left(-\left(\frac{\tau x^2}{4\lambda^2 t} + \frac{t}{\tau}\right)\right) \cdot \left(\frac{\tau^2 x^2}{4\lambda^4 t^{3/2}} - \frac{\tau}{2\lambda^2 \sqrt{t}}\right)}{2t\sqrt{\pi/\tau}} \tag{3.3}$$

4 - Calculating second derivative with respect to x multiplied by lambda squared:

$$\lambda^2 \frac{\partial^2 V}{\partial x^2} = \frac{\exp\left(-\left(\frac{\tau x^2}{4\lambda^2 t} + \frac{t}{\tau}\right)\right) \cdot \left(\frac{\tau^2 x^2}{4\lambda^2 t^{3/2}} - \frac{\tau}{2\sqrt{t}}\right)}{2t\sqrt{\pi/\tau}} = \tau \frac{\partial V}{\partial t} + V \tag{4.1}$$

Compute and plot (20 pts)

Compute and plot the spatial profile $V(x, t)$ for a few times t and similarly the time course $V(x, t)$ for a few locations x. Describe in a few words what is going on.

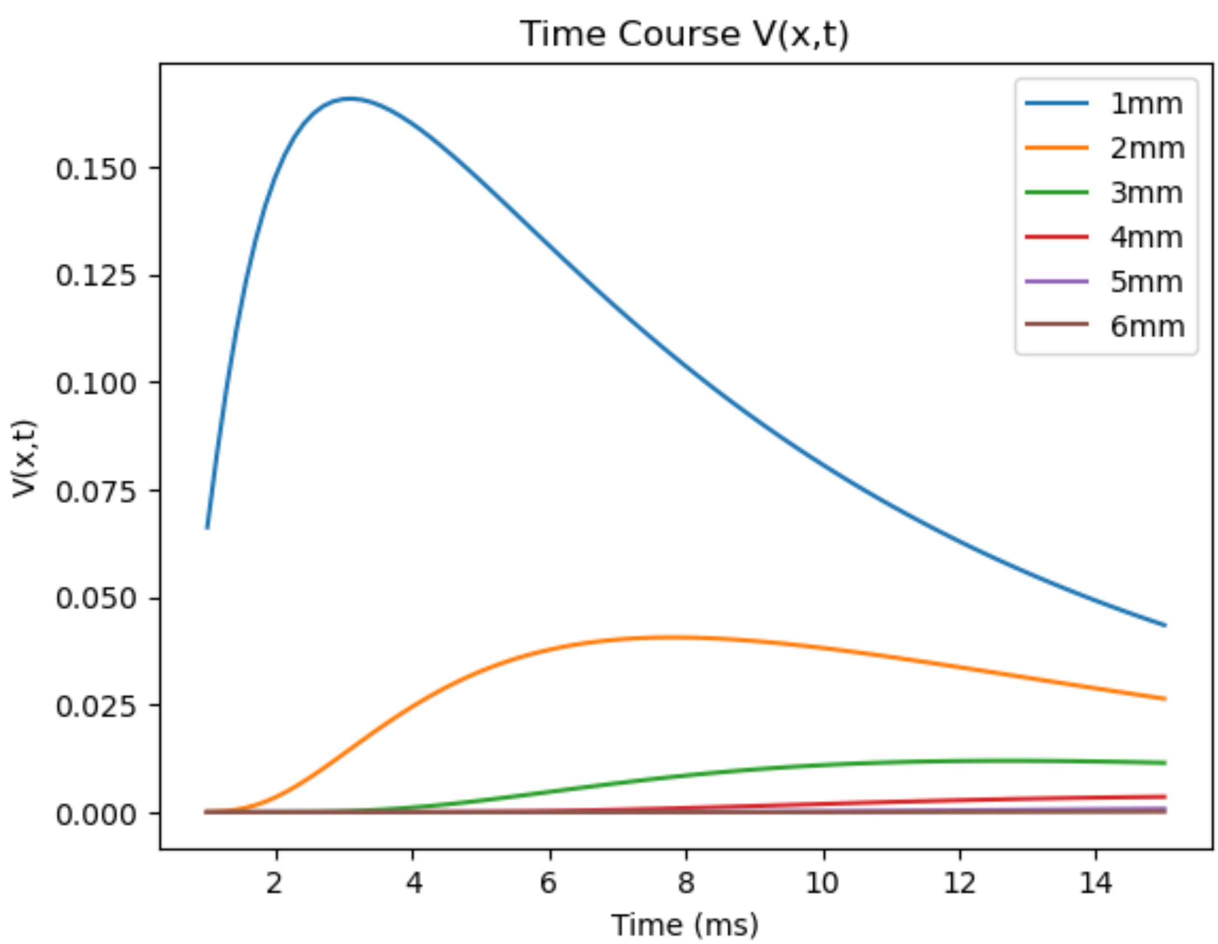
In [8]:
```
ort numpy as np
ort matplotlib.pyplot as plt


ime Course
 np.linspace(1,15, num=100)
= []

 x in range(1,7):
 Vs.append(1/np.sqrt(4*np.pi*t*1e-3/10e-3) * np.exp((-((10e-3)*(x*1e-3

 v in Vs:
 plt.plot(t, v)

.legend(["1mm", "2mm", "3mm", "4mm", "5mm", "6mm"])
.title("Time Course V(x,t)")
.ylabel("V(x,t)")
.xlabel("Time (ms)")
.show()
```



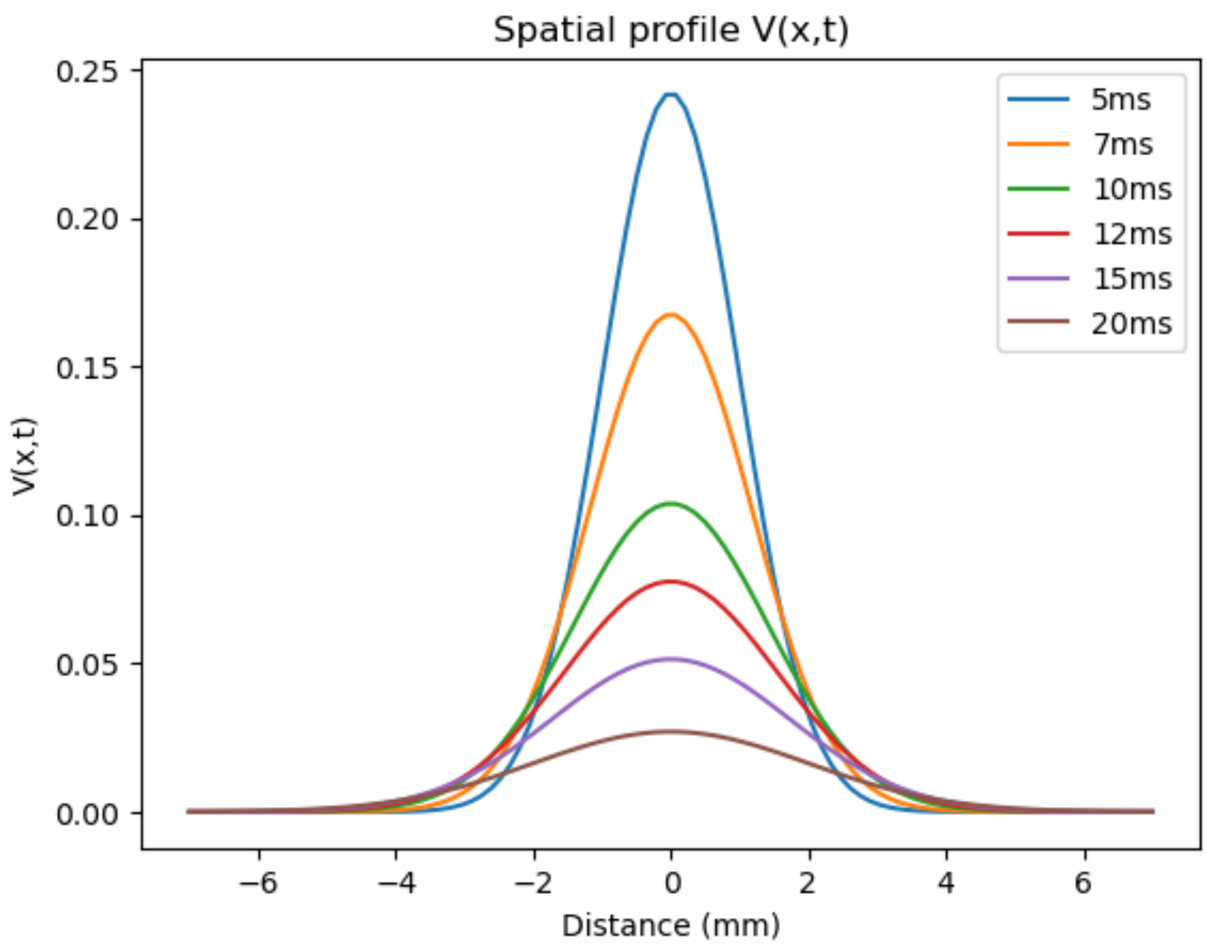
At a certain point, as time increases, the voltage drops, however a peak is seen shortly after t=0 where the measurement of voltage reaches its maximum. It appears that voltage reaches its max at a later time for distances further from the point of injection.

In [11]:
```
patial Profile
np.linspace(-7,7, num=100)
: []

t in [5, 7, 10, 12, 15, 20]:
Vs.append(1/np.sqrt(4*np.pi*t*1e-3/10e-3) * np.exp((-((10e-3)*(x*1e-3)

v in Vs:
plt.plot(x, v)

legend(["5ms", "7ms", "10ms", "12ms", "15ms", "20ms"])
title("Spatial profile V(x,t)")
ylabel("V(x,t)")
xlabel("Distance (mm)")
show()
```



```
As distance from the point that the voltage pulse occurs increases,
the voltage level itself decreases and likewise is seen in this plot
as time increases where you can see at different fixed times the
graph begins lower as the time increases.
```

Maximum time (10 pts)

How fast does the pulse propagate down the dendrite? For a given location x, at what time t_{max} does the pulse reach a maximum? How does that t_{max} depend on location x?

Hint: Read D&A (Dayan & Abbott book) for more on the topic.

The pulse seems to propagate on the order of milliseconds, and for a given location x we have the following as seen in Dayan & Abbott:

$$t_{max} = \frac{\tau}{4}\left(\sqrt{1+4\left(\frac{x}{\lambda}\right)^2} - 1\right)$$

This tells us that:

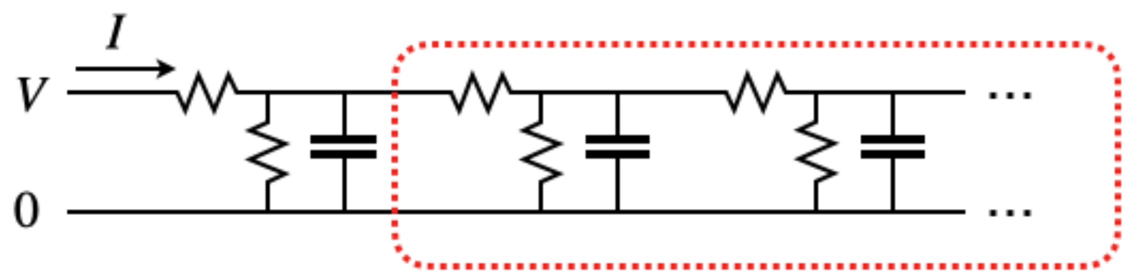
$$t_{max} \propto x$$

Bonus question: How many hours did you spend on this problem set? (1 pt)

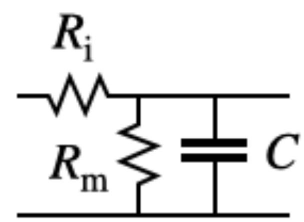
```
8 hours
```

Bonus question: Impedance of an infinite dendrite (20 pts)

What is the impedance of an infinite dendrite: If we apply an intracellular voltage V at one end, how much current I will flow into the dendrite?



Short segment of length ΔL :



$$R_i = r_i \frac{\Delta L}{\pi a^2} \qquad R_m = \frac{r_m}{2\pi a\,\Delta L} \qquad C = c_m\, 2\pi a\,\Delta L$$

Hints:

a) Think of the dendrite as a "ladder" of resistors and capacitors corresponding to short segments of membrane (see Figure).

b) Start simple: Assume the voltage is constant and we are looking for the constant current after everything has settled into steady state. That means we can ignore the capacitors, because no capacitive current flows when the voltages are constant.

c) Notice that the part of the cable inside the dotted box has the same impedance as the whole thing (why?).

d) Use what you know about resistors in parallel and in series to solve for the impedance of the infinite cable.

For further reading see e.g. Christof Koch, Biophysics of Computation, Ch 2.

$Note\ that\ hint\ (c)\ tells\ us\ Z_{total} = Z_{red}$

$Additionally,\ we\ need\ not\ consider\ the\ impedance\ from\ capacitors\ during\ steady\ st$

$$R_{total} = R_I + \left(\frac{1}{R_m} + \frac{1}{R_{red}}\right)$$

$$R_{red} = R_I + \frac{1}{R_m} + \frac{1}{R_{red}}$$

$$R_{red} - \frac{1}{R_{red}} = R_I + \frac{1}{R_m}$$

$$R_{red} - \frac{1}{R_{red}} = r_i \frac{\Delta L}{\pi a^2} + \frac{2\pi a \Delta L}{r_m}$$

$$R_{red} - \frac{1}{R_{red}} = \frac{r_i r_m \Delta L + 2\pi^2 a^3 \Delta L}{r_m \pi a^2}$$

$$R_{red}^2 - 1 = R_{red} \cdot \frac{r_i r_m \Delta L + 2\pi^2 a^3 \Delta L}{r_m \pi a^2}$$

$$R_{red}^2 - R_{red} \cdot \frac{r_i r_m \Delta L + 2\pi^2 a^3 \Delta L}{r_m \pi a^2} - 1 = 0$$

$Let\ c := \frac{r_i r_m \Delta L + 2\pi^2 a^3 \Delta L}{r_m \pi a^2}:$

$$R_{red}^2 - c \cdot R_{red} - 1 = 0$$

$$R_{red} = \frac{c \pm \sqrt{c^2 + 4}}{2}$$

The value of c is always positive in a practical sense, so subtracting $\sqrt{c^2+4}$ from c when $\sqrt{c^2+4} > c$ means a negative resistance which is not possible:

$$R_{red} = \frac{c + \sqrt{c^2 + 4}}{2}$$

$V = IR:$

$$I = \frac{V}{R_{red}} = \frac{V}{\frac{c+\sqrt{c^2+4}}{2}} = \frac{2V}{c + \sqrt{c^2+4}} = \frac{2V}{\frac{r_i r_m \Delta L + 2\pi^2 a^3 \Delta L}{r_m \pi a^2} + \sqrt{\left(\frac{r_i r_m \Delta L + 2\pi^2 a^3 \Delta L}{r_m \pi a^2}\right)^2 + 4}}$$