Harvard-MIT Division of Health Sciences and Technology
HST.131: Introduction to Neuroscience
Course Director: Dr. David Corey

The Action Potential

Short Review Session (about 15 slides)

One Review Problem (about 15 slides)

Review for HST131/N200
B M Hooks
25 Sep 05

The Generic HST130/N200 Exam
Four Pieces of Advice from Mac:

(1) Write your name on EVERY page.

(2) Short answer means SHORT answer. (space provided)

(3) Leave no questions blank (unless you intend to)

(4) Multiple choice:
Circle ALL that apply
… versus …
Circle THE BEST answer

Example:
Chromosomes contain which of the following? Circle ALL that apply:
a. Protein
b. Nucleic Acid
c. Obi-Wan Kenobi
d. Lipid rafts

Last Bit of Advice

Please study hard for the exam.

It will be difficult. The questions will address a variety of levels of knowledge, ranging from the very general (which everyone will know) to the very specific (which fewer people will know).

The exam is intended to be challenging, making it unlikely that everyone will have a perfect score.

Material and Gratuitous Neuroanatomy Plug

Our material in the first block is somewhat less clinical and more basic science that that which follows in neuroanatomy. (HST)

Neuroanatomy will have a rapid pace and cover a lot of material:

-Please do a good job the lab assignments, as they aid understanding of the material and the lab

-The first neuroanatomy lab has an assignment and may occur on the Friday following the exam.

How Does Myelin Affect Conduction Velocity?

$$\text{Length Constant: } \lambda = \sqrt{r_m/r_i}$$

$$r_m = R_m/2\pi a$$

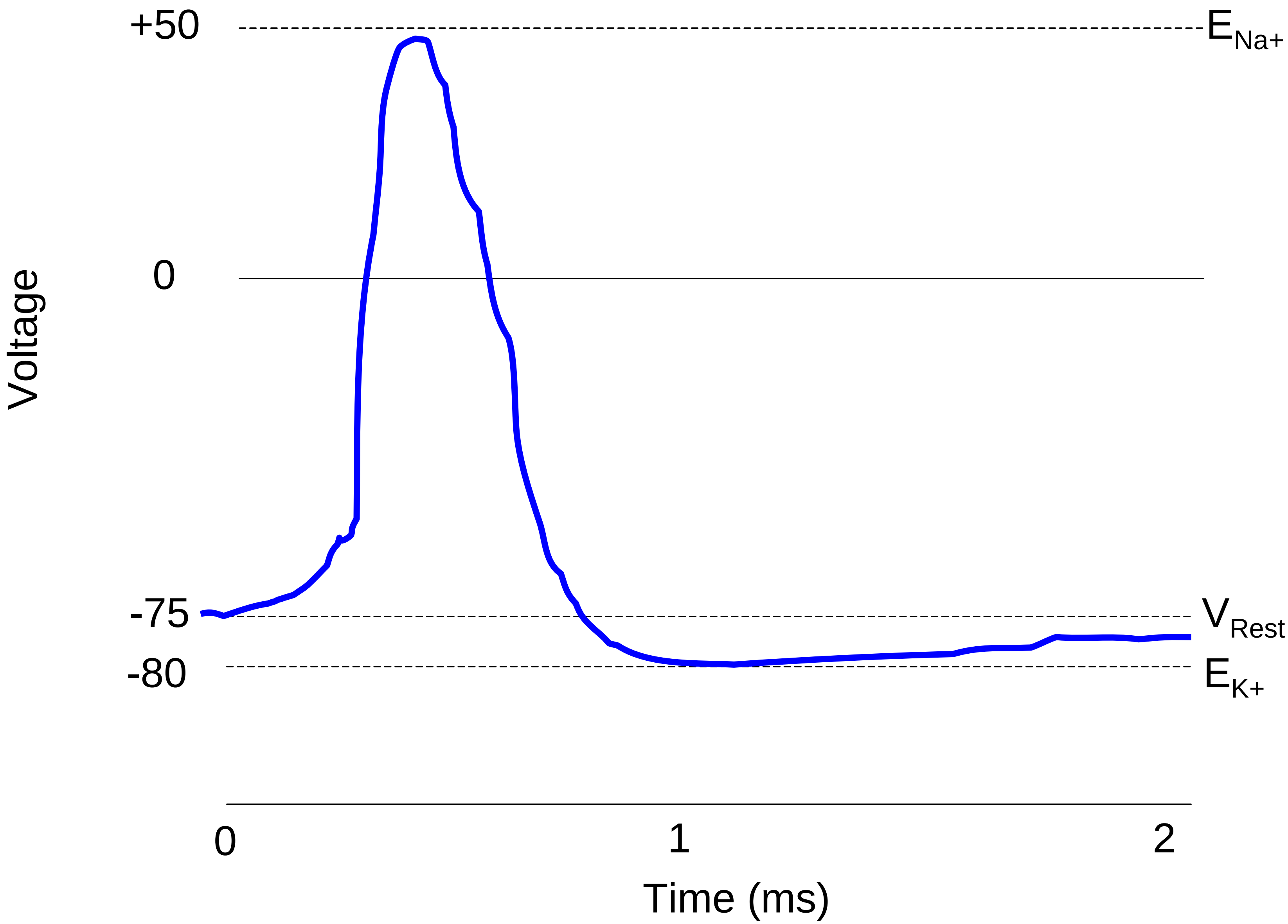
$$r_i = R_i/\pi a^2$$

$$c_m = C_m 2\pi a$$

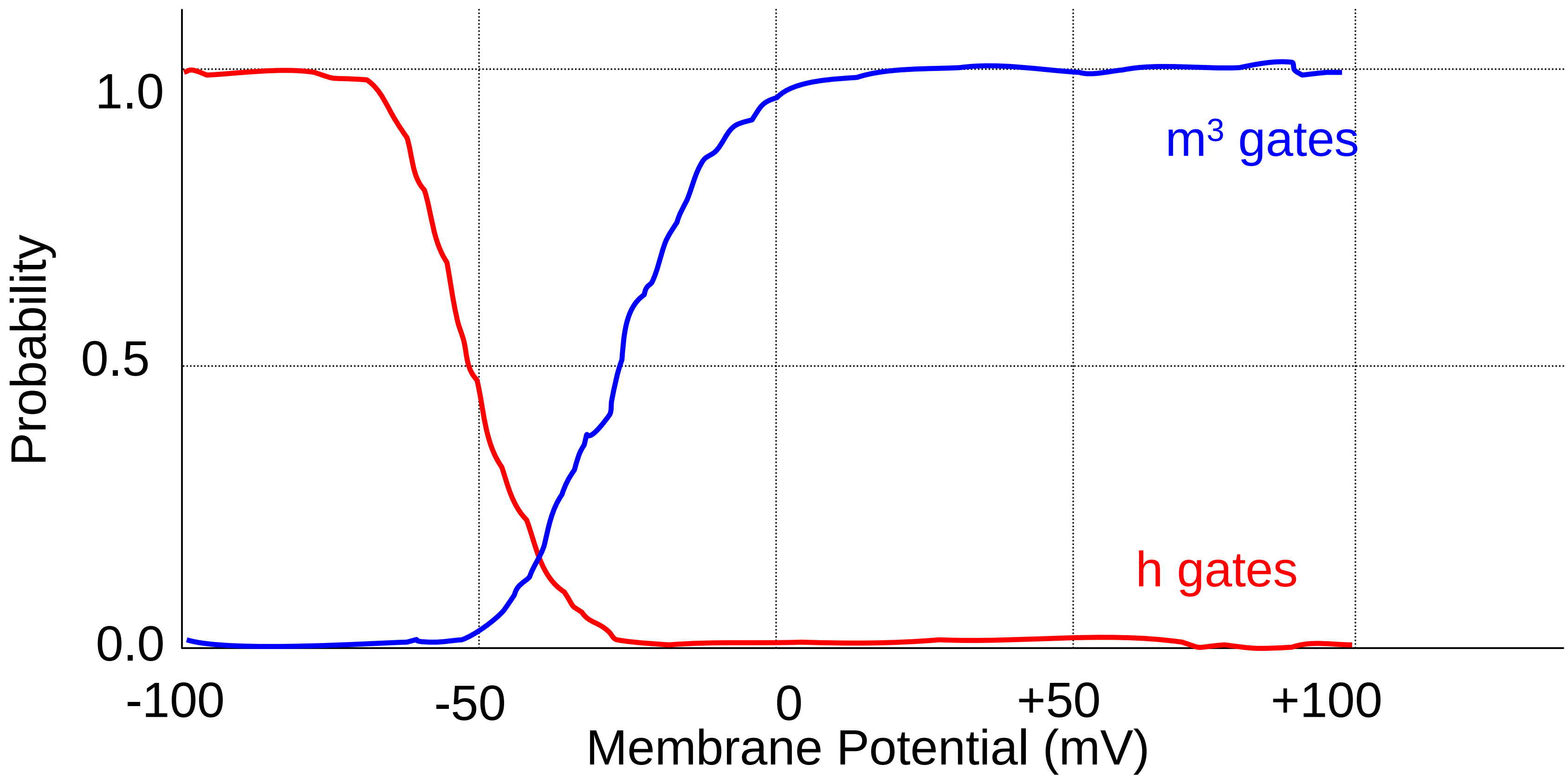
$$\text{Velocity: } v \text{ (proportional to) } \sqrt{(aD)/(2R_iC_m)}$$

D = Channel Density

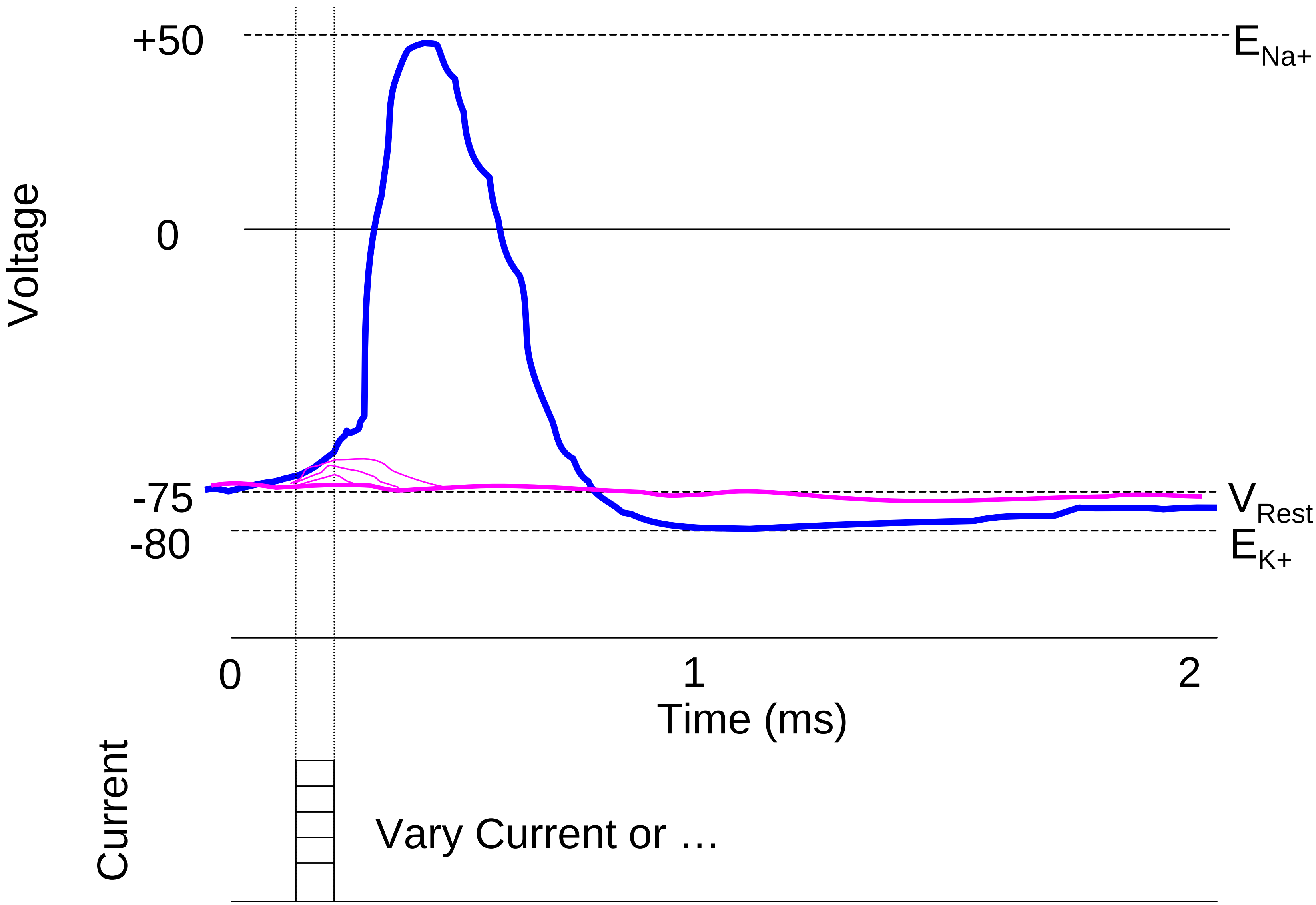
The basic Action Potential drawing



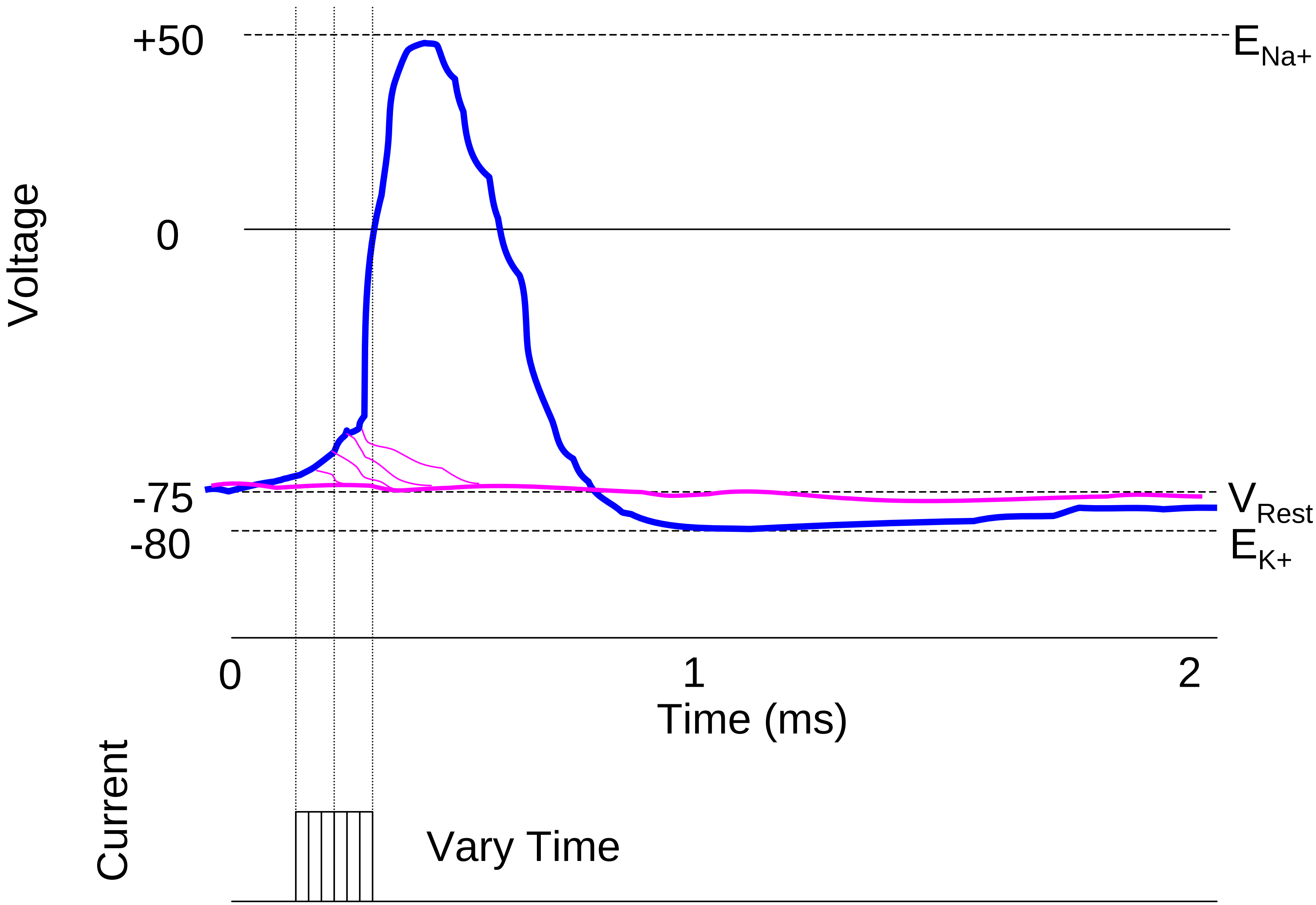
The basic gates drawing for sodium currents



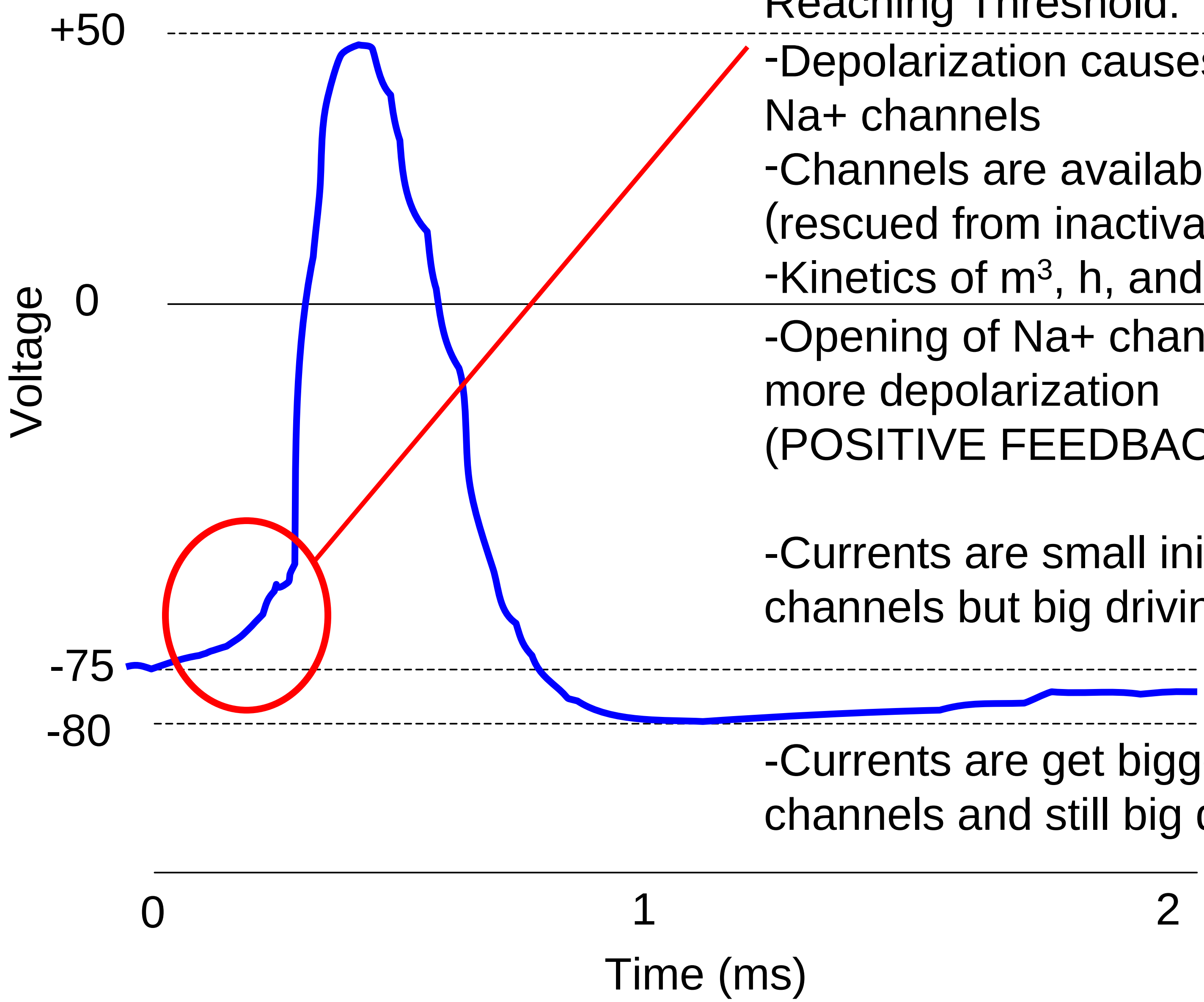
Voltage Protocol ("Experiment") to Test Threshold



Voltage Protocol (“Experiment”) to Test Threshold



What's Happening at Each Point of the AP?



Reaching Threshold:

-Depolarization causes opening of Na+ channels

-Channels are available at rest (rescued from inactivation)

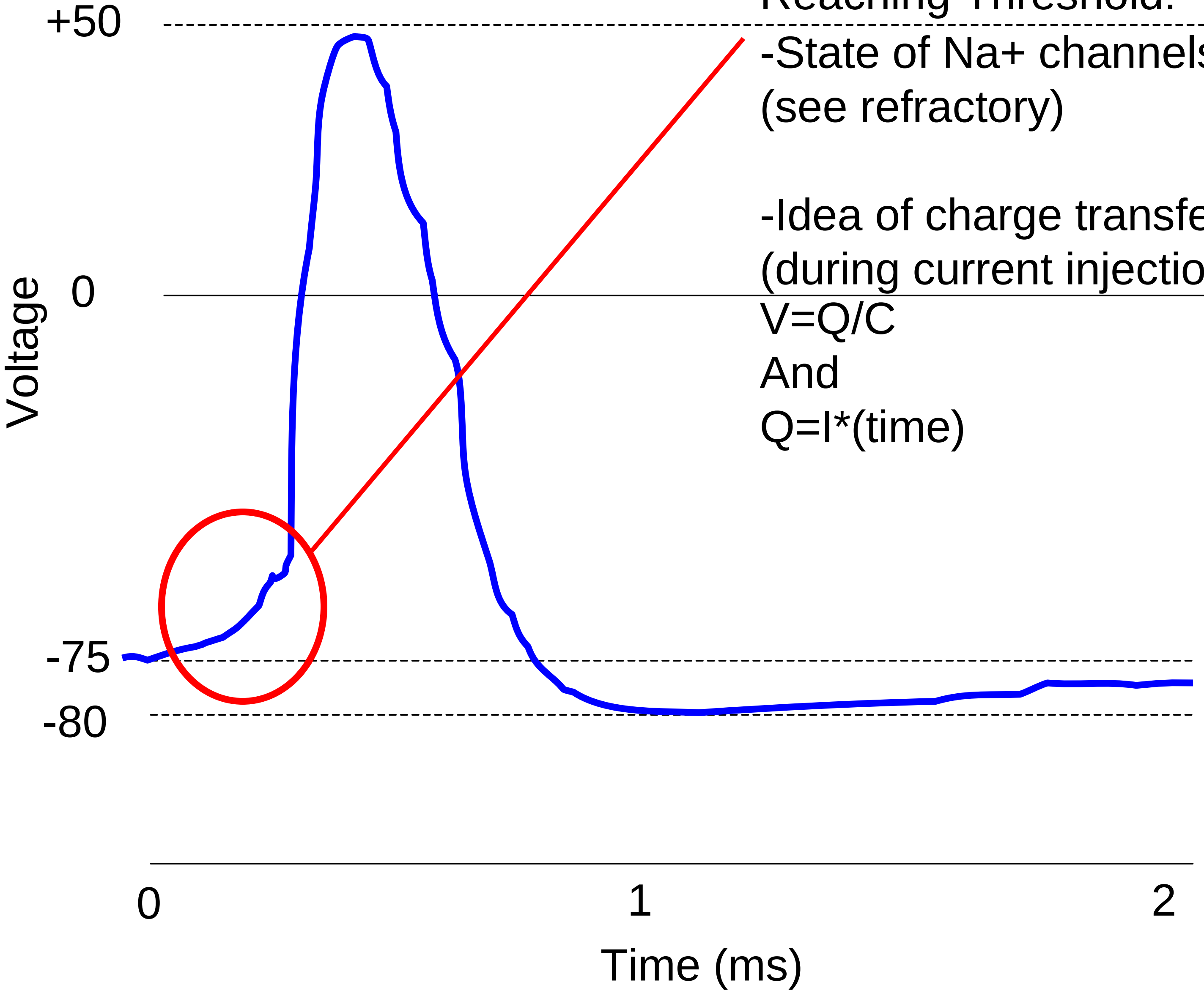
-Kinetics of m^3, h, and n^4 gates

-Opening of Na+ channels causes more depolarization (POSITIVE FEEDBACK)

-Currents are small initially (few open channels but big driving force)

-Currents are get bigger (more open channels and still big driving force)

What's Happening at Each Point of the AP?



Reaching Threshold:

-State of Na+ channels at rest is key (see refractory)

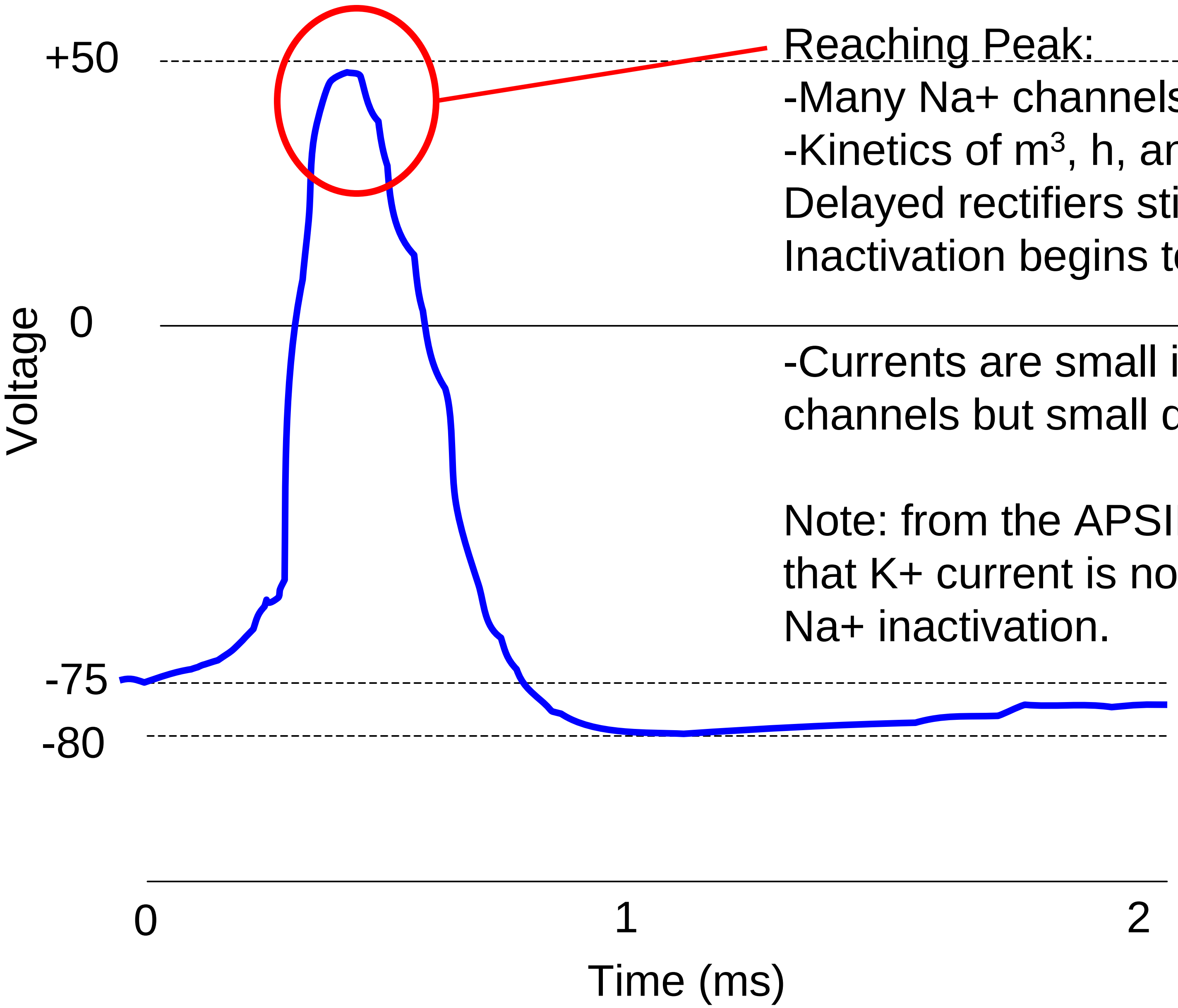
-Idea of charge transfer (during current injection):

$V=Q/C$

And

$Q=I*(\text{time})$

What's Happening at Each Point of the AP?



<u>Reaching Peak:</u>

-Many Na+ channels open

-Kinetics of m^3, h, and n^4 gates:

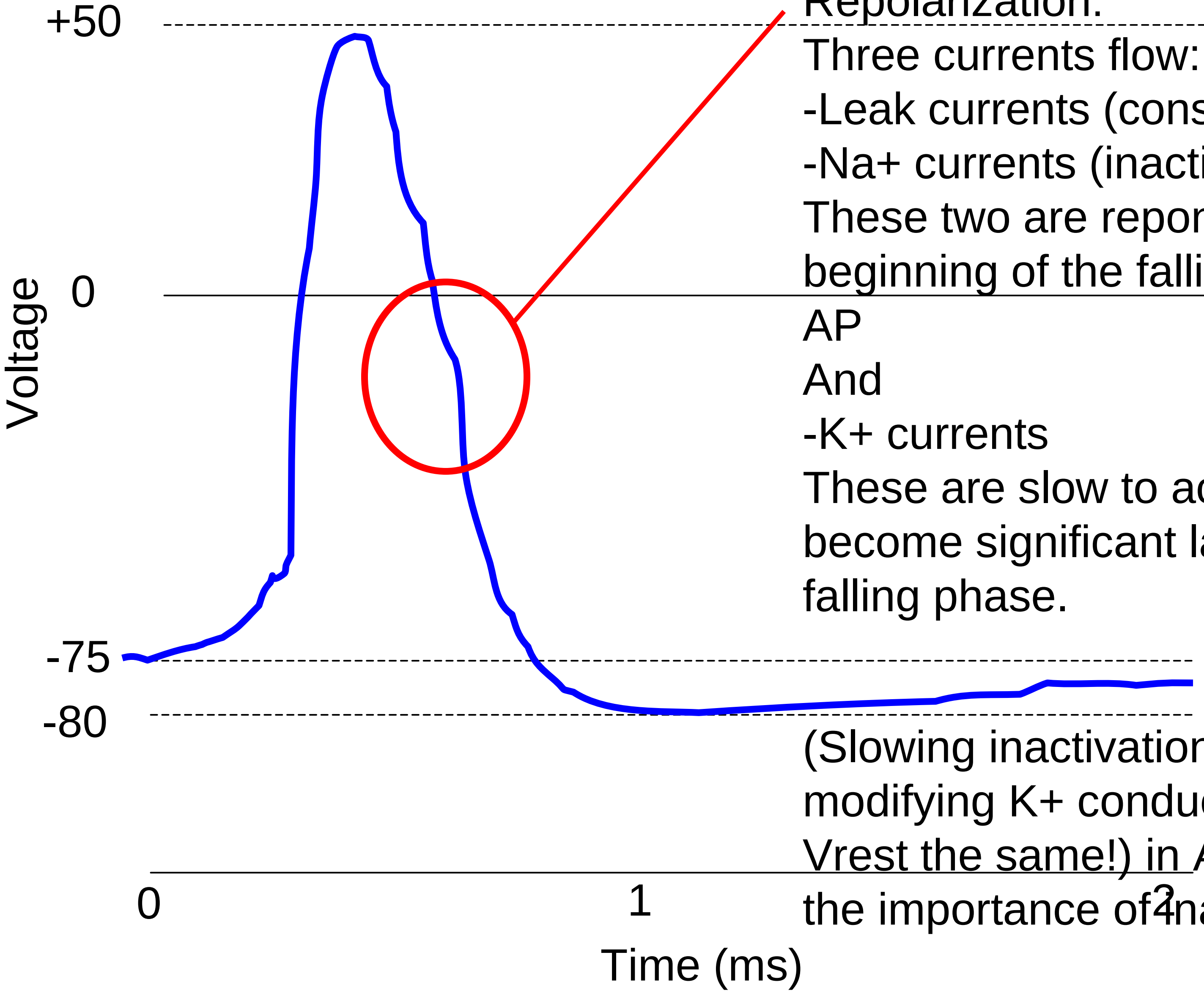
Delayed rectifiers still not yet on

Inactivation begins to close channels

-Currents are small initially (many open channels but small driving force)

Note: from the APSIM model, we see that K+ current is not as important as Na+ inactivation.

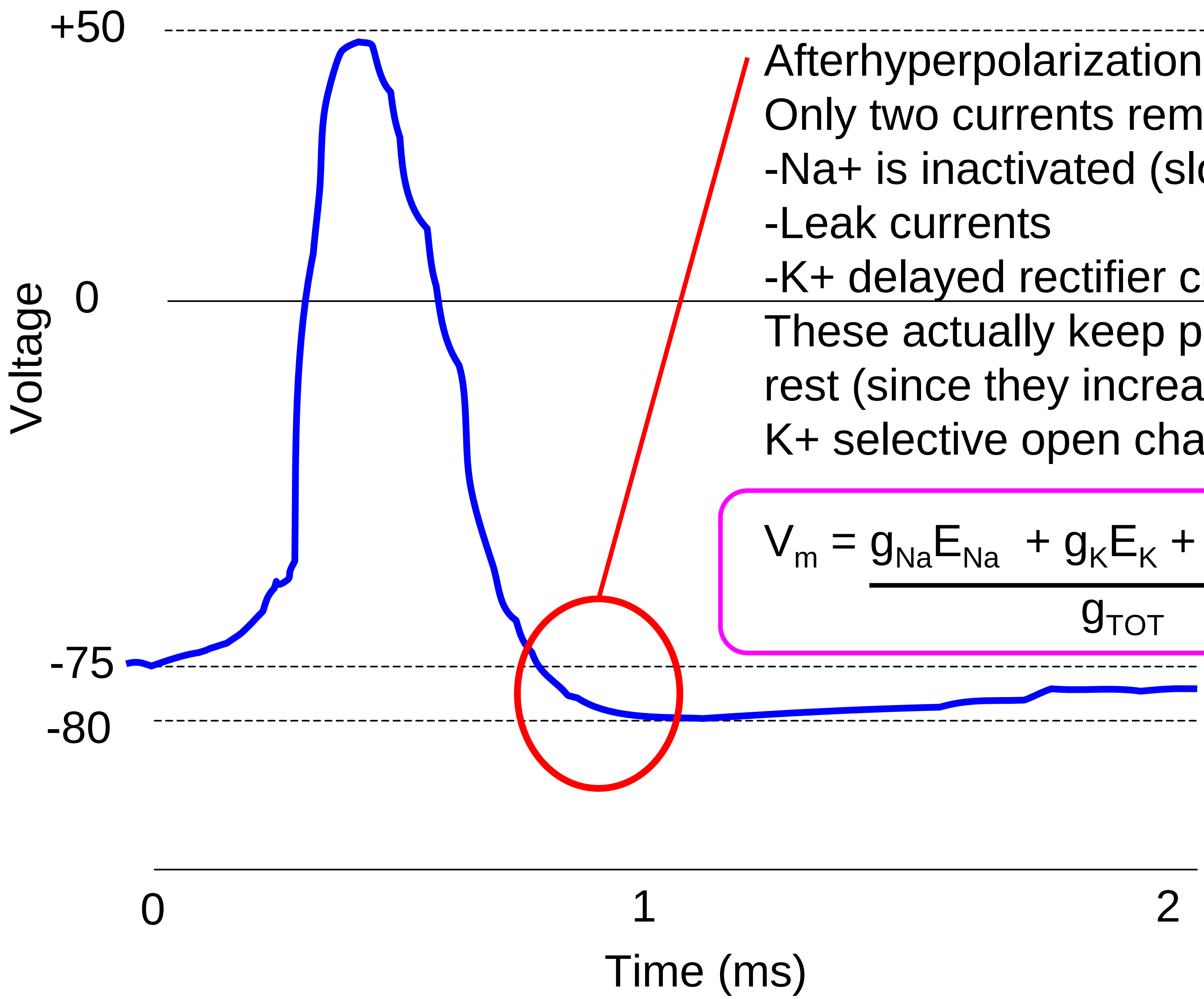
What's Happening at Each Point of the AP?



Repolarization:
Three currents flow:
-Leak currents (constant)
-Na+ currents (inactivating)
These two are reponsible for the beginning of the falling phase of the AP
And
-K+ currents
These are slow to activate and so become significant later during the falling phase.

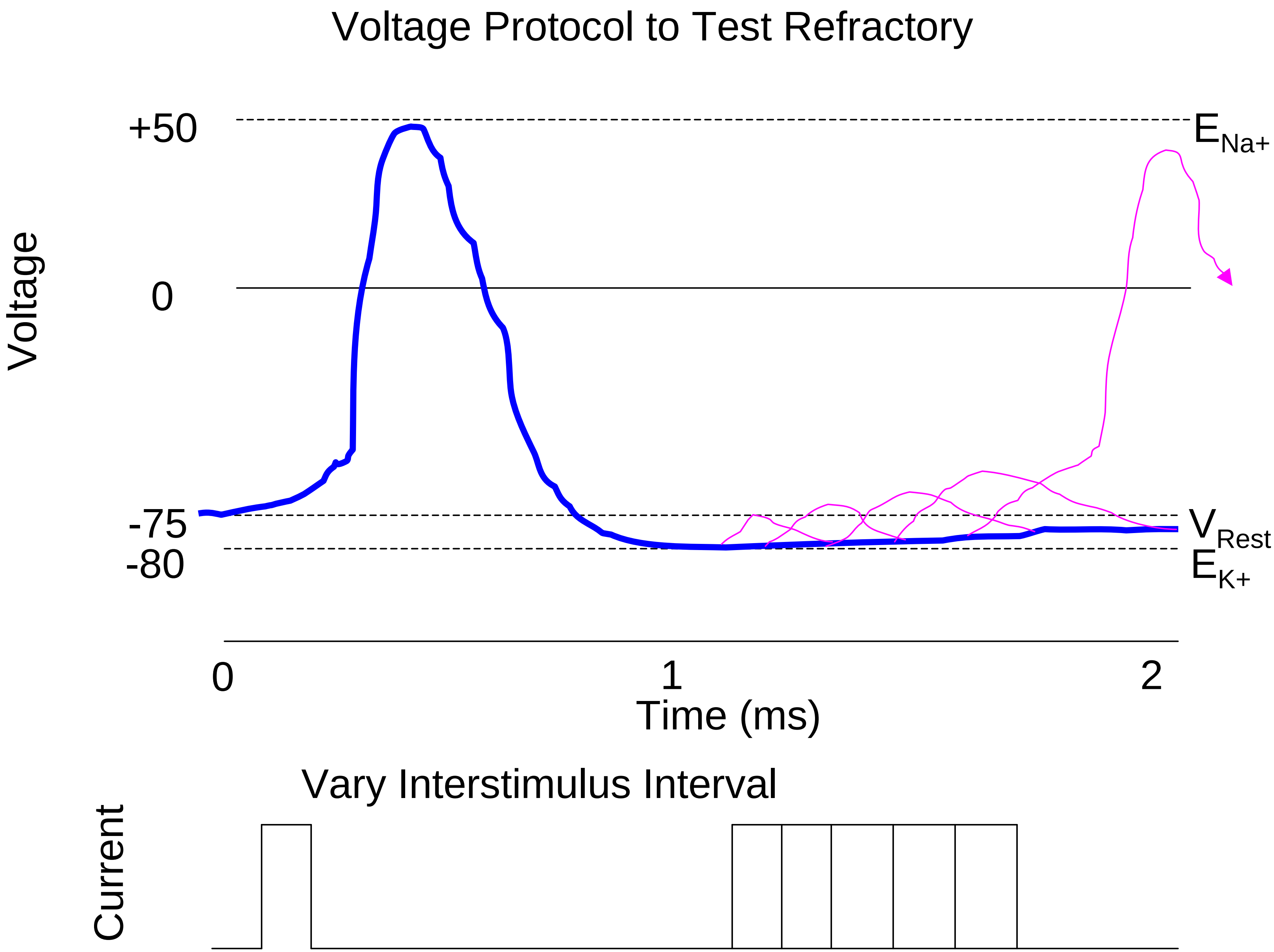
(Slowing inactivation and separately modifying K+ conductance (but keep Vrest the same!) in APSIM shows the importance of inactivation.)

What's Happening at Each Point of the AP?

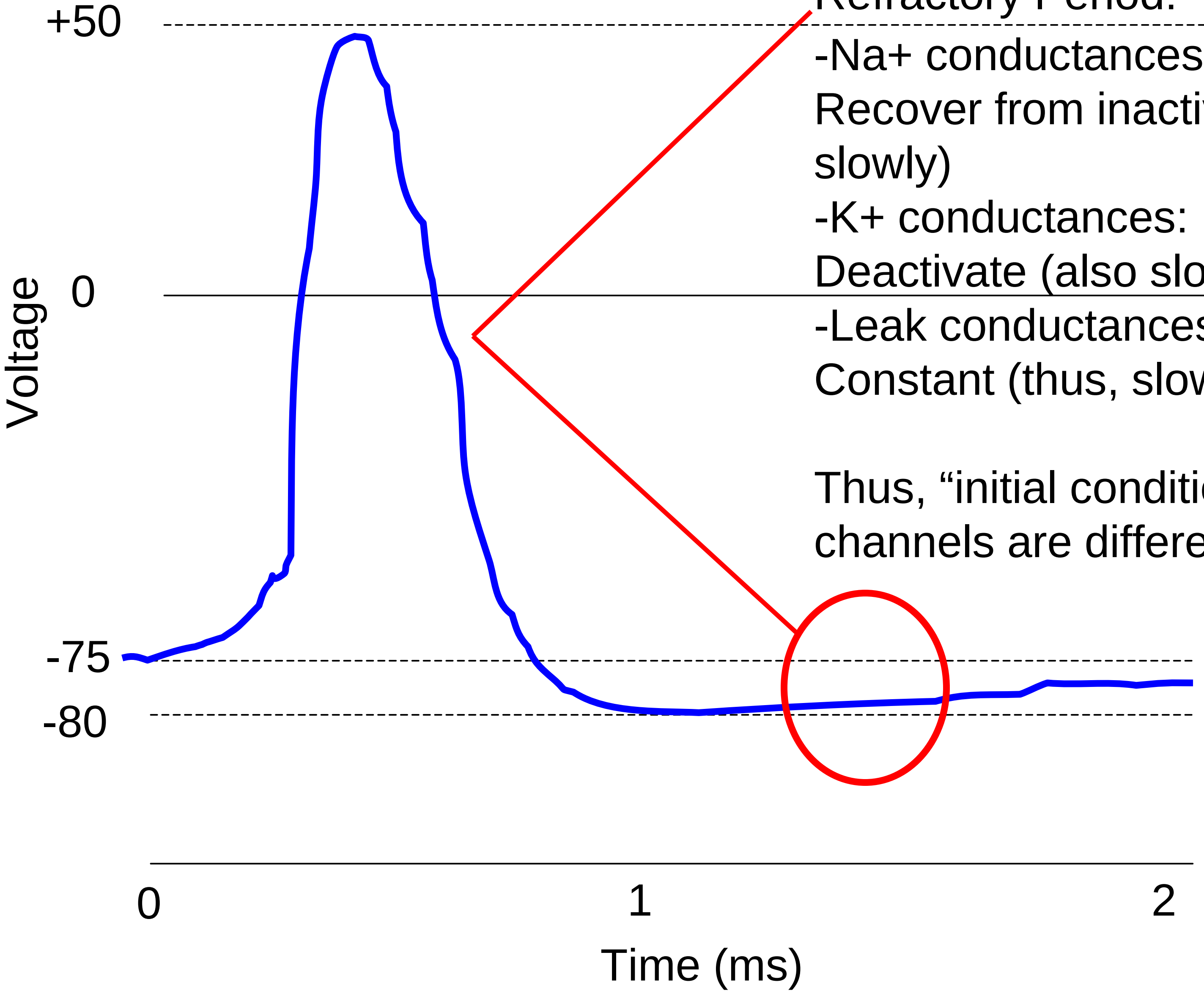


Afterhyperpolarization:
Only two currents remain:
-Na+ is inactivated (slow recovery)
-Leak currents
-K+ delayed rectifier currents
These actually keep potential below rest (since they increase the fraction of K+ selective open channels).

$$V_m = \frac{g_{Na}E_{Na} + g_K E_K + \ldots}{g_{TOT}}$$


Voltage Protocol to Test Refractory
+50
0
-75
-80
Voltage
E Na+
V Rest
E K+
0
1
2
Time (ms)
Vary Interstimulus Interval
Current

What’s Happening at Each Point of the AP?



Refractory Period:

-Na+ conductances:
Recover from inactivation (but slowly)

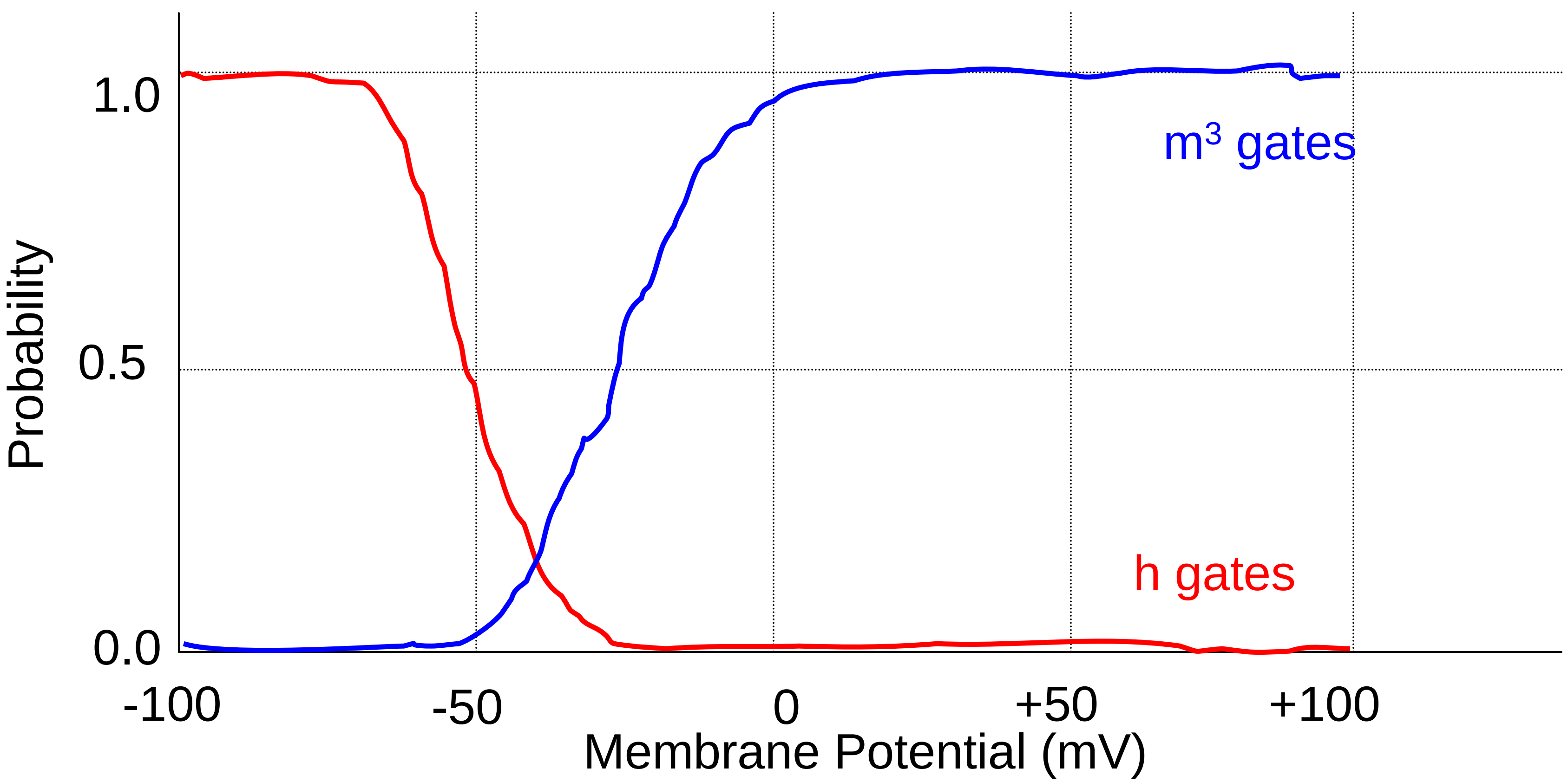
-K+ conductances:
Deactivate (also slowly)

-Leak conductances:
Constant (thus, slow return to rest)

Thus, “initial conditions” of available channels are different!

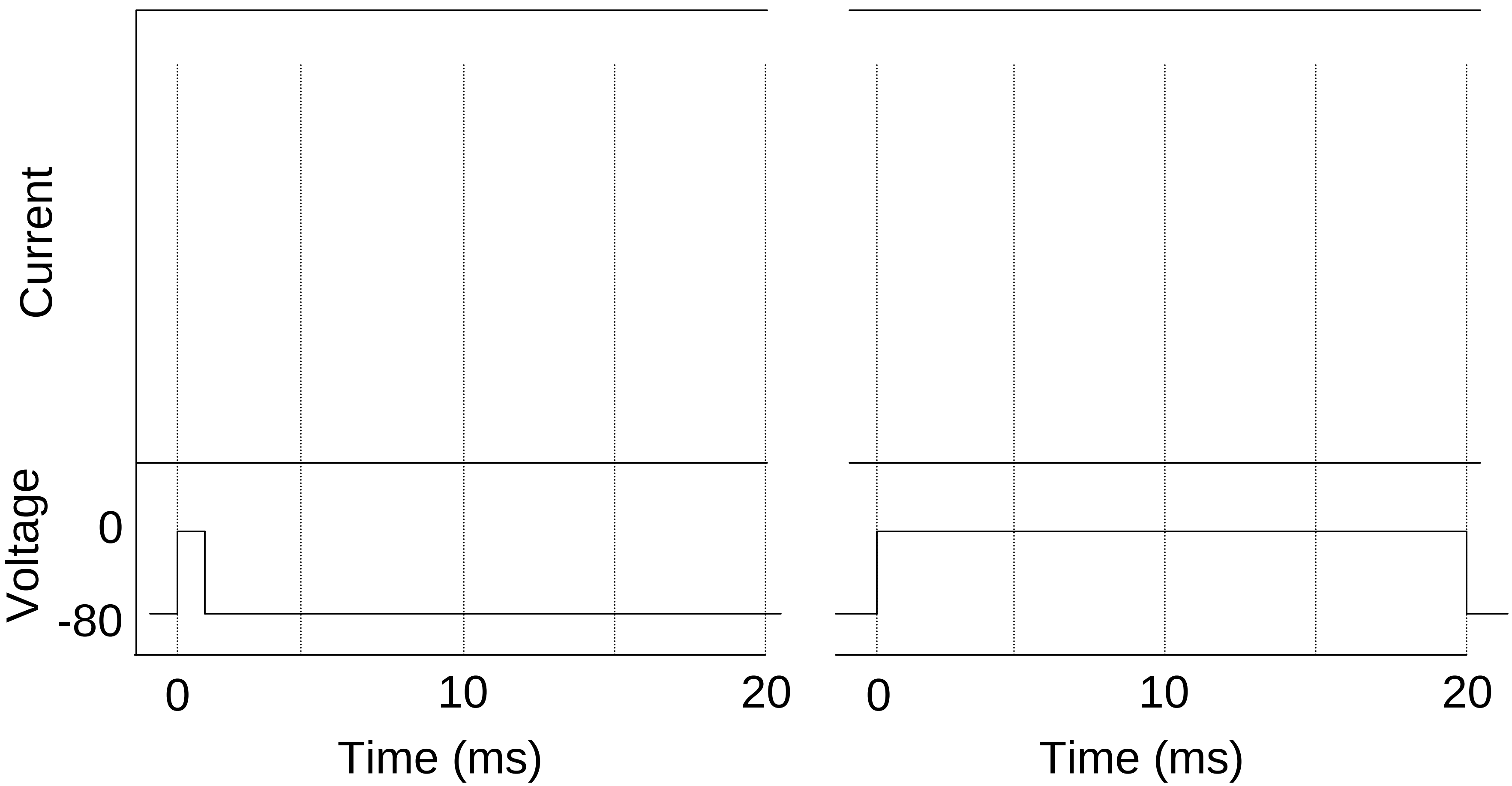
Sample Question:

A voltage clamp experiment was performed in which a neuron was stepped from –80 mV to 0 mV and then back to –80 mV (the protocols are shown). The P(V) curves for the "m^3" gate and "h" gate are shown below. The time constants of activation and inactivation are 0.5 and 5 msec, respectively.



How study sodium current alone?

Draw the sodium current in response to the following voltage steps. Assume peak Na+ conductance is 120nS and reversal potential for sodium is +40mV:



Potentially Helpful Equations:

$I = N_{channels} * \gamma_{channel} * P_{open} * (V_m - V_{reversal})$

$I = G_{max} * P_{open} * (V_m - V_{reversal})$

And, if $P_{open} = 1.0$, then $I=I_{max:}$

$I_{max} = G_{max} * (V_m - V_{reversal})$

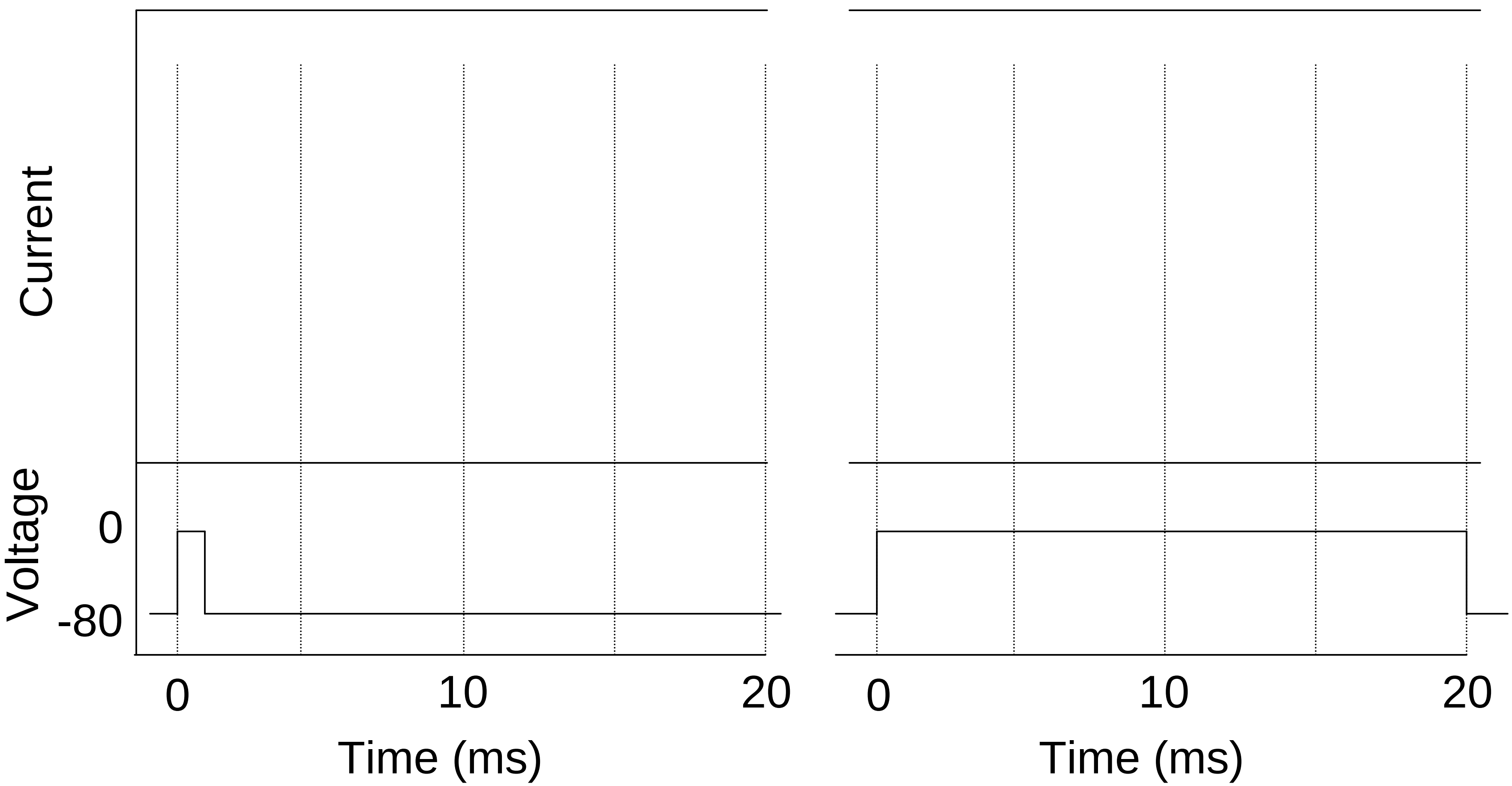
Determine peak Na+ current using I=V/R=VG.

At 0mV, -40mV driving force and 120nS conductance.

I_{max}=-4.8nA. (Negative since Na+ will be inward current.)

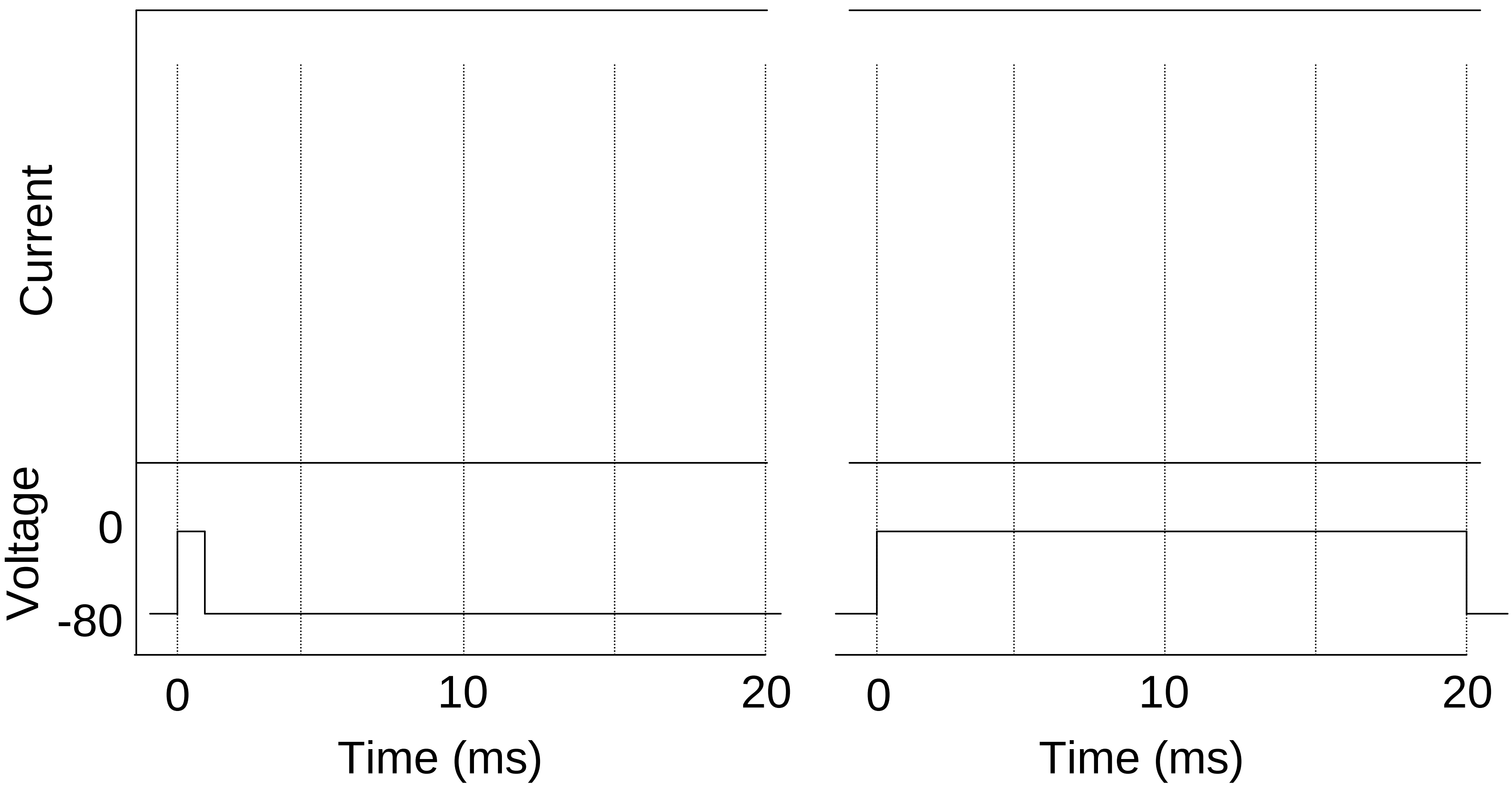
At -80mV, -120mV driving force and 120nS conductance.

I_{max}=-14.4nA.



Determine initial current.

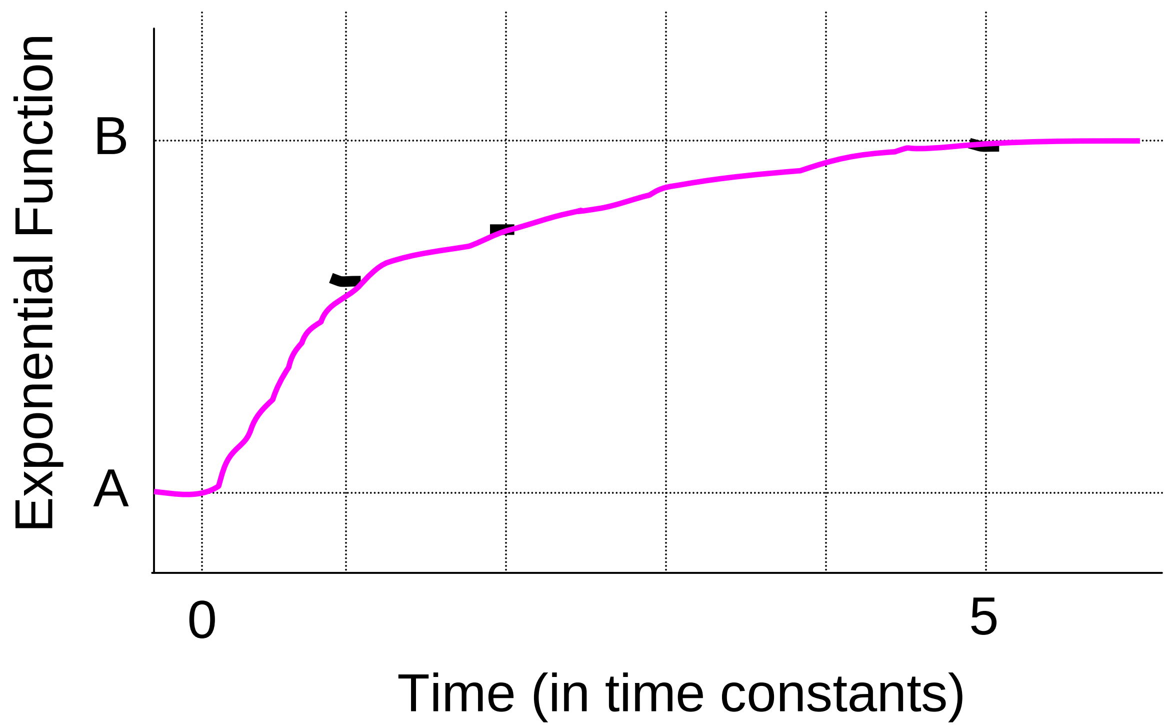
Since we assume the clamp has been at -80mV for a long time before the recording, h gates are all open (P=1.0) and m^3 gate are all closed (P=0.0). Thus, open probability is zero and there is no current.



Now step to +0mV. The steady state open probability is about 1.0 for m^3 and 0.0 for h gates. However, it will take a certain amount of time to reach these probabilities.

-Using the time constant, we see that, after 1ms is: 2 time constants for m^3 (so $1-e^{-t/tau} = 1-e^{-2} = 0.86$) and 1/5th time constants for h (so $e^{-t/tau} = e^{-0.2} = 0.81$).

-Thus, P_{open} at 1ms is (0.86)*(0.81)=.70



$F(t)=B+(A-B)(e^{-t/tau})$

From the graph, we take:
For m^3, A=0 and B=1.
For h, A=1 and B=0.

1 tau = 63%

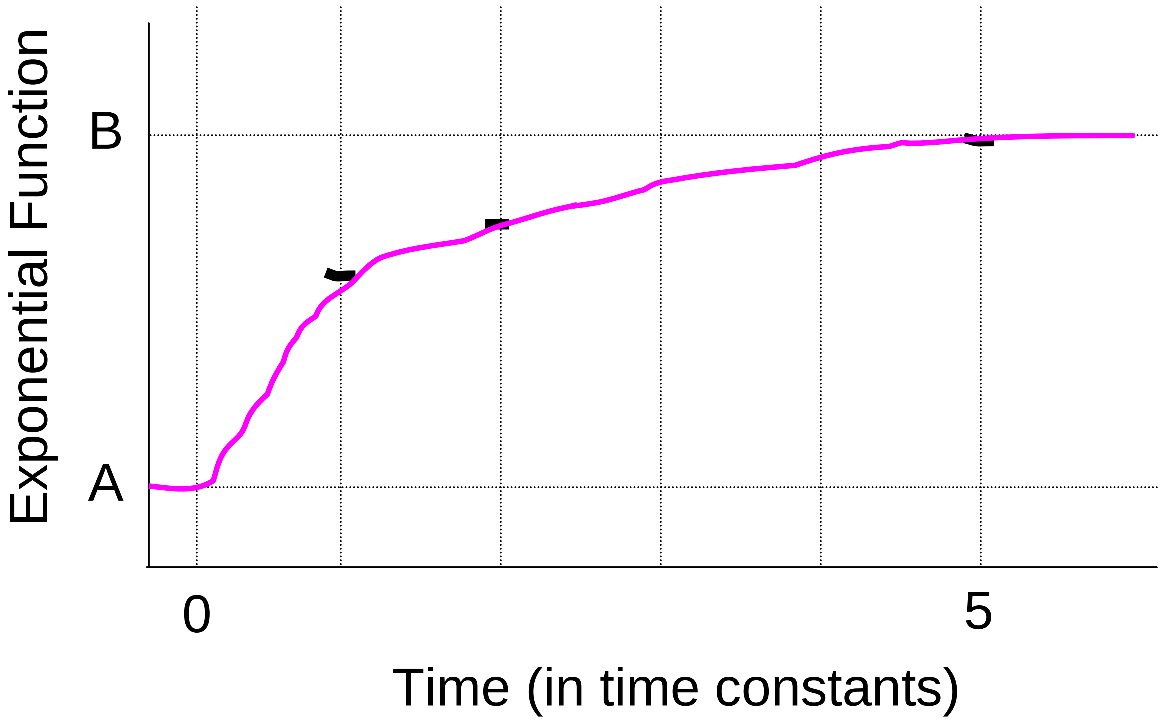
2 tau = 86%

5 tau = 99%

Now step to +0mV. Use a similar strategy for 20ms. The steady state open probability is about 1.0 for m^3 and 0.0 for h gates. However, it will take a certain amount of time to reach these probabilities.

-Using the time constant, we see that, after 20ms is: 40 time constants for m^3 (so $1-e^{-t/tau} = 1-e^{-40} = 1.00$) and 4 time constants for h (so $e^{-t/tau} = e^{-4} = 0.02$).

-Thus, P_{open} at 1ms is (1.00)*(0.02)=.02



$F(t)=B+(A-B)(e^{-t/tau})$

From the graph, we take:
For m^3, A=0 and B=1.
For h, A=1 and B=0.

1 tau = 63%

2 tau = 86%

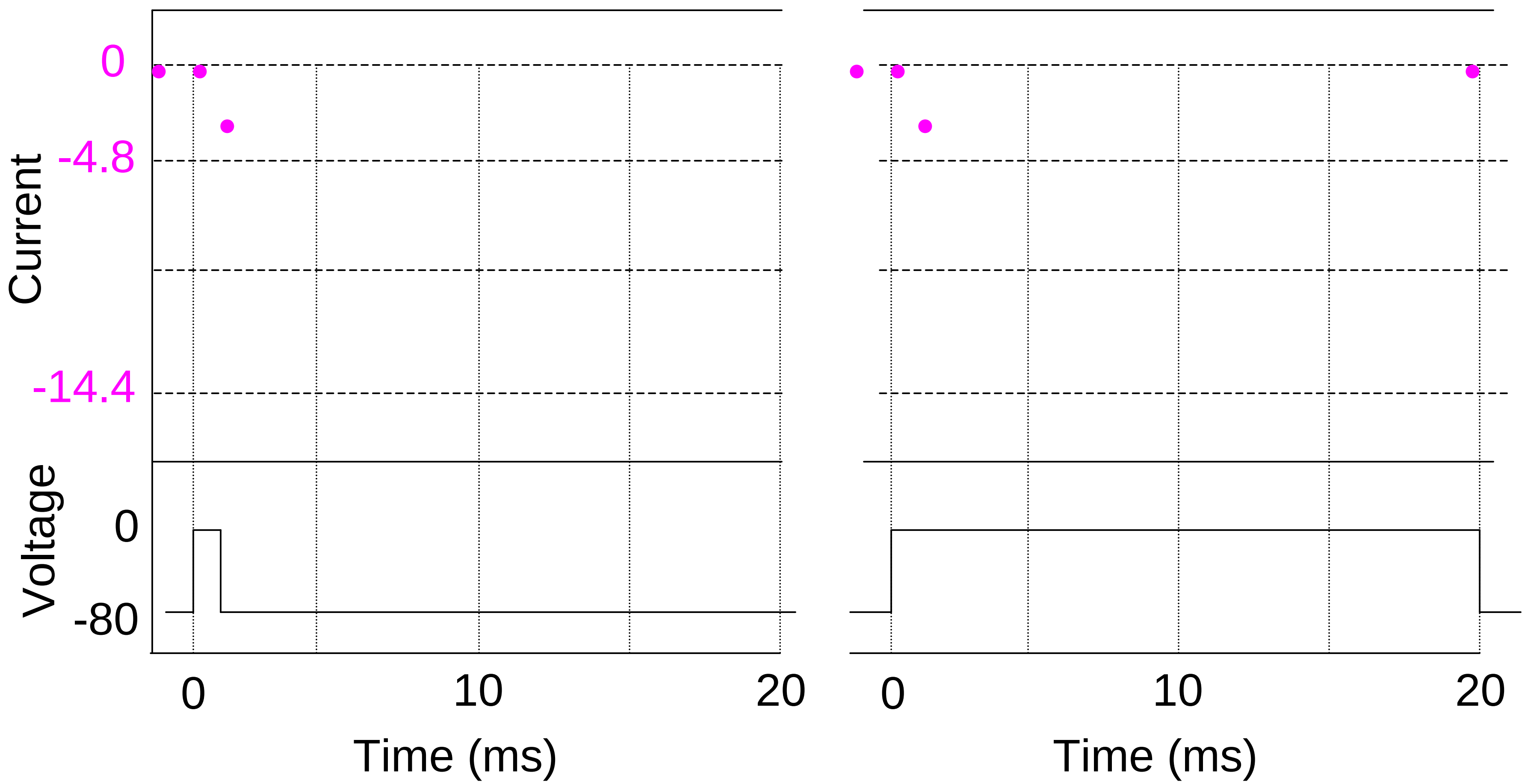
5 tau = 99%

Update plot for maximal currents and calculated currents at three time points:

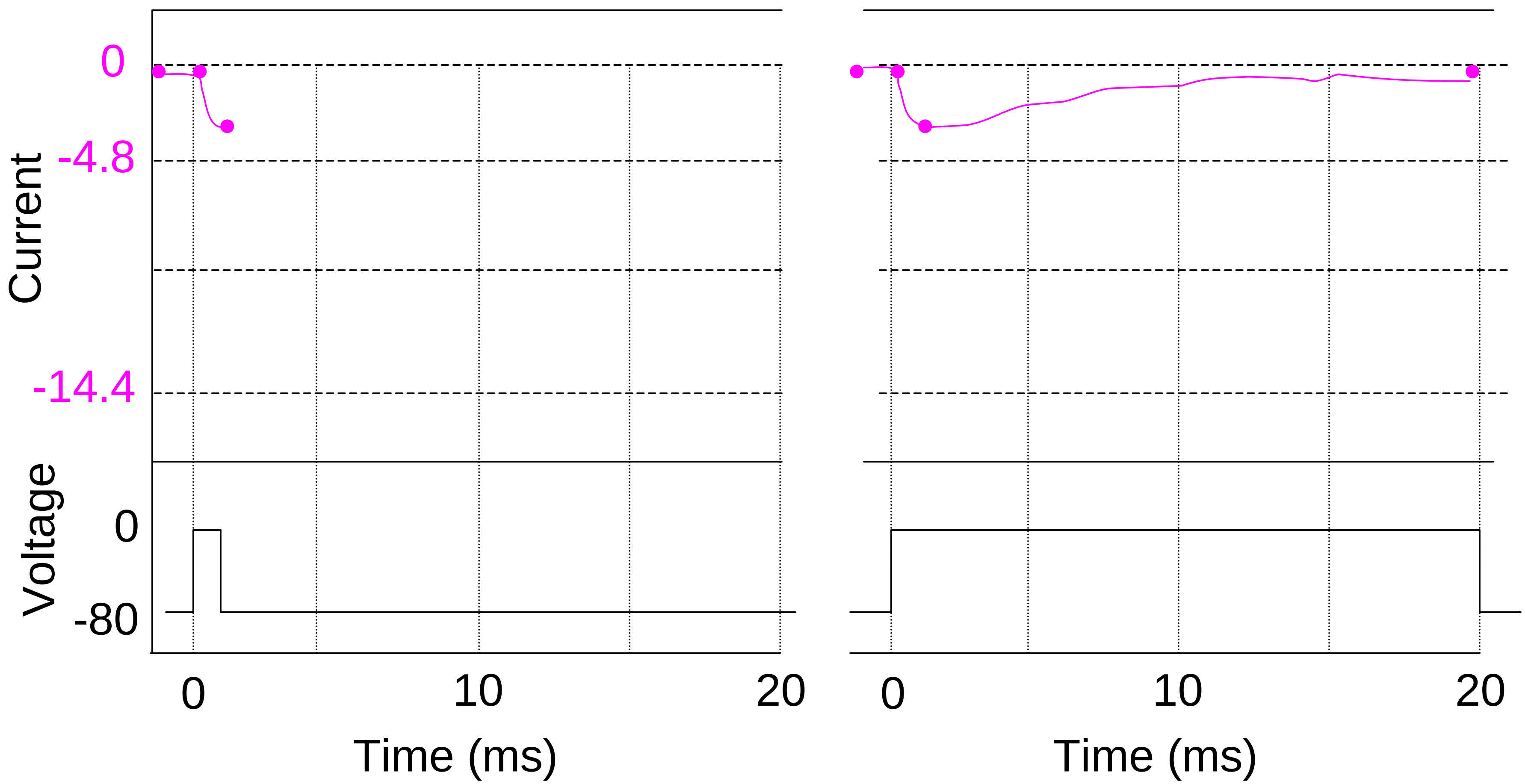
t=0ms: 0.00 of max

t=1ms: 0.70 of max (at 0mV) (0.7)*(-4.8)=3.36

t=20ms: 0.02 of max (at 0mV) (0.02)*(-4.8)=0.10



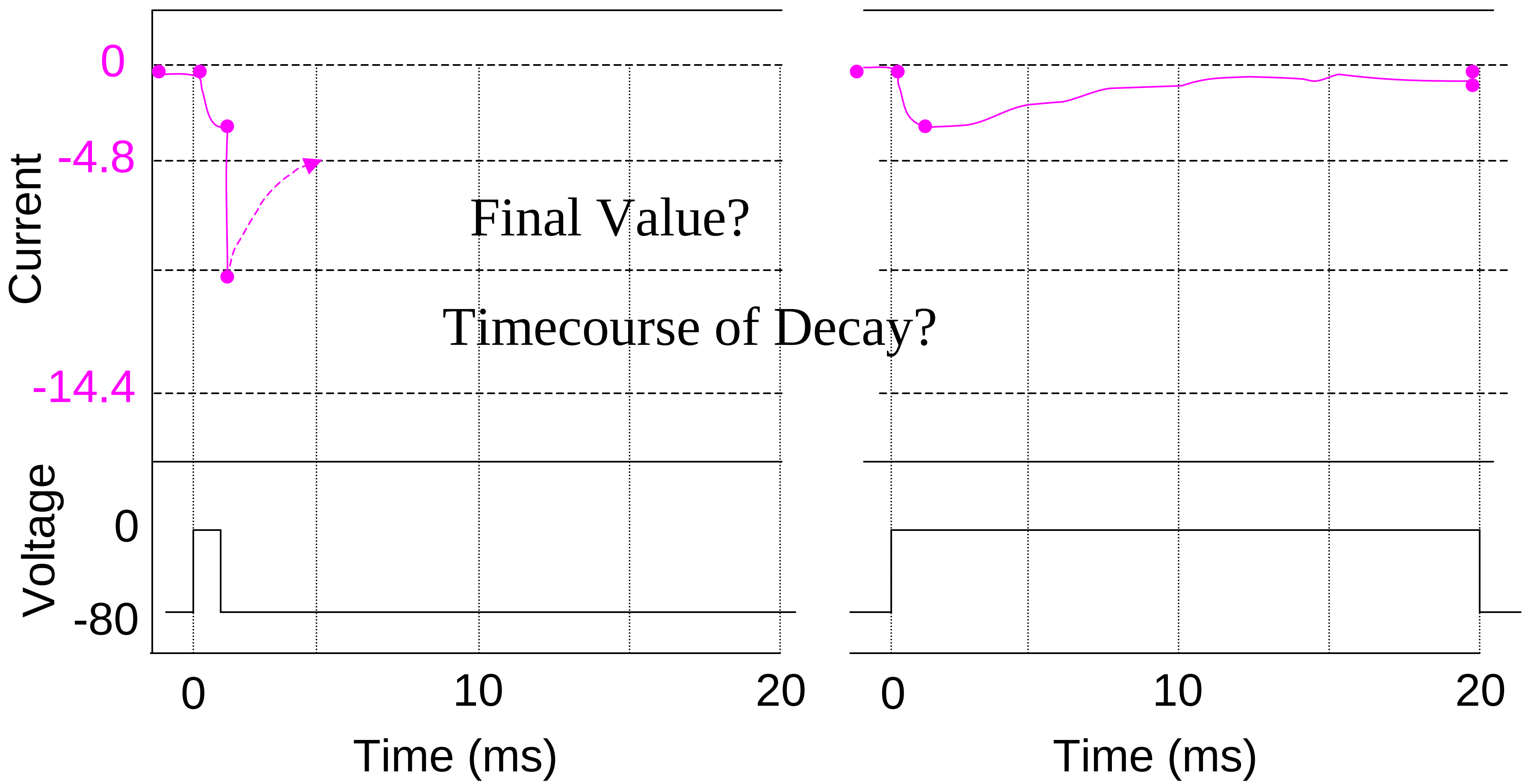
Sketch in the currents.
What happens after we step back to -80mV?



At -80mV, maximal current changes instantly with the driving force, but P_{open} does not instantly change

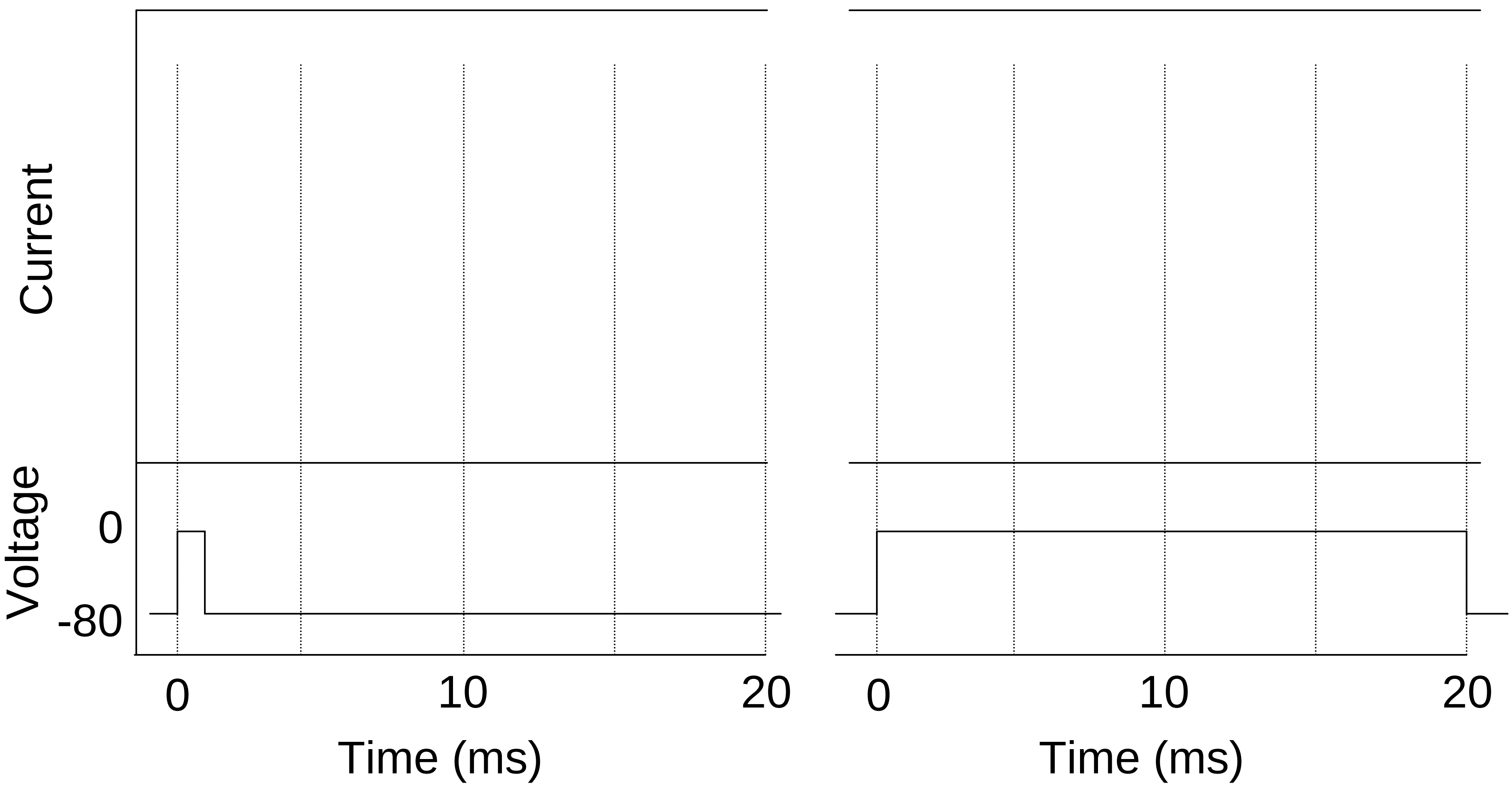
t=1ms: 0.70 of max (at -80mV) (0.7)*(-14.4)=10.08

t=20ms: 0.02 of max (at -80mV) (0.02)*(-14.4)=0.29



Now we apply a drug that prevents inactivation.
Now draw the current over time for the following voltage steps.

This makes it easier …

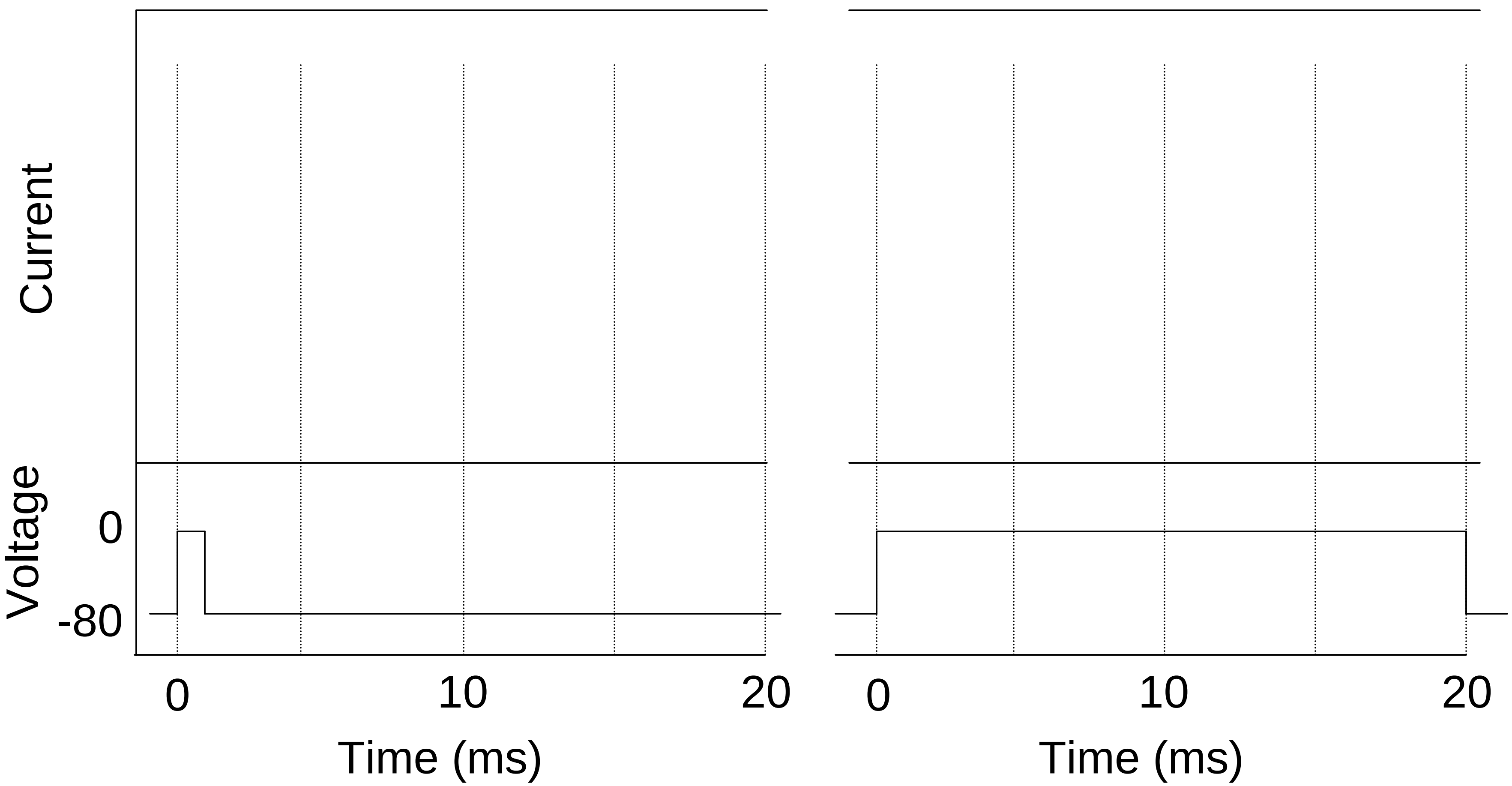


This makes it easier …

P_{open} is now the same as the m^3 probability (already calculated).

Removing inactivation does not affect I_{max} (already calculated).

So …

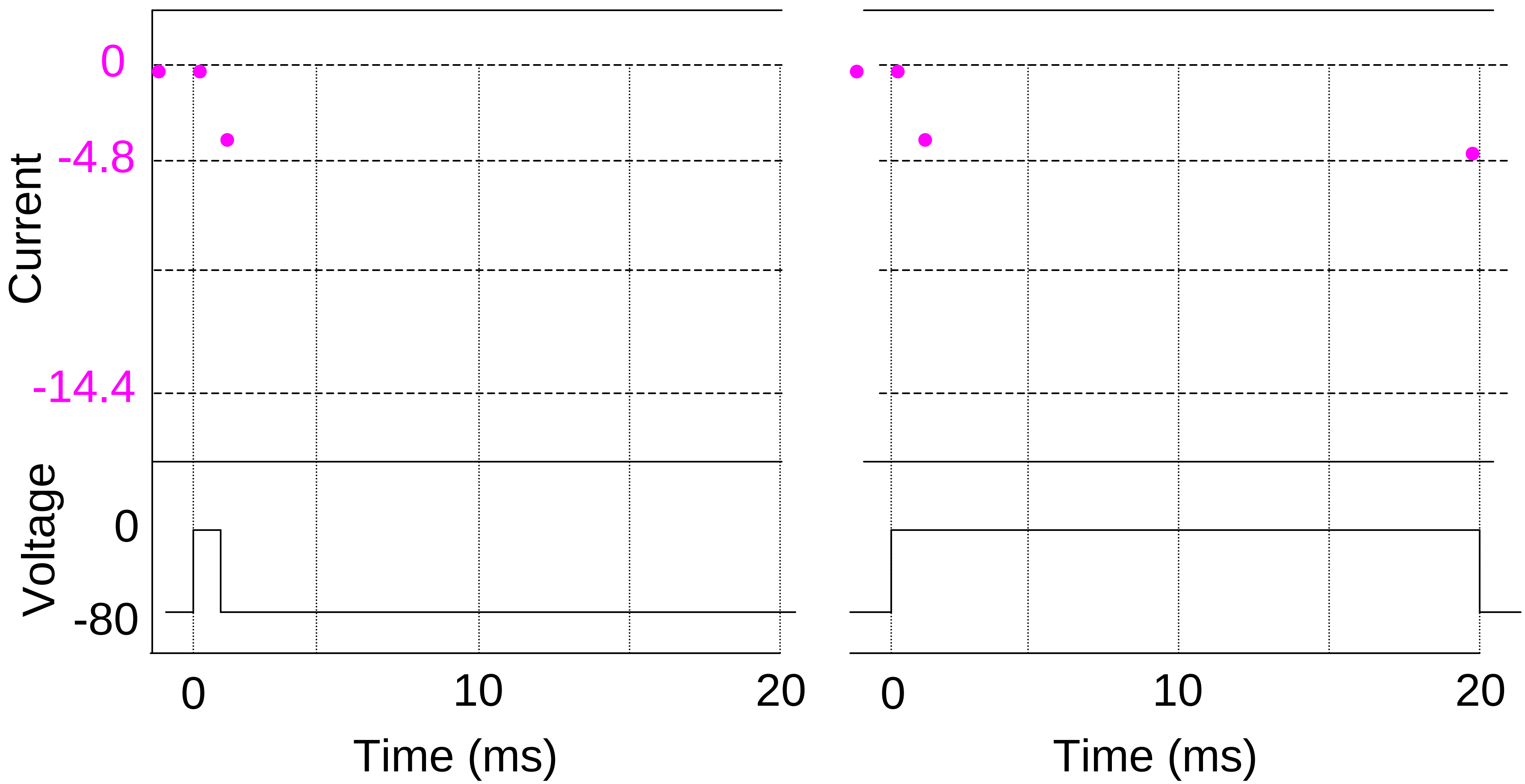


Update plot for maximal currents and calculated currents at three time points:

t=0ms: 0.00 of max

t=1ms: 0.86 of max (at 0mV) (0.86)*(-4.8)=-4.13

t=20ms: 1.00 of max (at 0mV) (1.00)*(-4.8)=-4.8



And add the points following the step to -80mV.
At -80mV, maximal current changes instantly with the driving force, but P_{open} does not instantly change.
t=1ms: 0.86 of max (at -80mV) (0.86)*(-14.4)=-12.38
t=20ms: 1.00 of max (at -80mV) (1.00)*(-14.4)=-14.4