AMATH 422 HW 5 Submission

I Dwell time distributions: theory.

Consider an ion channel with 4 open states and 2 closed states. Give a mathematical argument, similar to that in class, that derives the typical functional form of the dwell time distribution for the channel being in any one of the open states. Note: I am looking for a derivation here, not just a statement of the answer or a "mantra" or result from class.

Four open states (S_1, S_2, S_3, S_4) Two closed states (S_5, S_6)

$\Omega = \{Open, Closed\} = \{S_1, S_2, S_3, S_4, S_5, S_6\}$

Indistinguishable between S and the other open states

We want to find the mathematical arguement for the dwell time: P(Dwell time in (C_1, C_2, C_3, C_4) for k steps)

We are going to assume time is homogenous and time does not affect the markov chain probabilities. We are going to assume the gate starts in the open condition $X_0 \in \{Open\}$

Want to find the probabiltiy Open for K steps $P(T_o >= k)$

We know that the probablity of going to other open steps is $Ap_0 = p_1$ Only interested in open states

$$\begin{bmatrix} a_{11} & a_{12} & a_{13} & a_{14} & a_{15} & a_{16} \\ a_{21} & a_{22} & a_{23} & a_{24} & a_{25} & a_{26} \\ a_{31} & a_{32} & a_{33} & a_{34} & a_{35} & a_{36} \\ a_{41} & a_{42} & a_{43} & a_{44} & a_{45} & a_{46} \\ a_{51} & a_{52} & a_{53} & a_{54} & a_{55} & a_{56} \\ a_{61} & a_{62} & a_{63} & a_{64} & a_{65} & a_{66} \end{bmatrix} \begin{bmatrix} p_1(0) \\ p_2(0) \\ p_3(0) \\ p_4(0) \\ 0 \\ 0 \end{bmatrix} = \begin{bmatrix} p_1(1) \\ p_2(1) \\ p_3(1) \\ p_4(1) \\ p_5(1) \\ p_6(1) \end{bmatrix}$$

We can remove the two right columns due to the zeros in p(0) we can remove the bottom two row because those would release us from the dwell time. Simplifying becomes

$$\begin{bmatrix} a_{11} & a_{12} & a_{13} & a_{14} \\ a_{21} & a_{22} & a_{23} & a_{24} \\ a_{31} & a_{32} & a_{33} & a_{34} \\ a_{41} & a_{42} & a_{43} & a_{44} \end{bmatrix} \begin{bmatrix} p_1(0) \\ p_2(0) \\ p_3(0) \\ p_4(0) \end{bmatrix} = \begin{bmatrix} p_1(1) \\ p_2(1) \\ p_3(1) \\ p_4(1) \end{bmatrix}$$

This holds for k and k+1 steps because

$$P^c_{1,2,3,4}(k) = P(X_k = S_i | X_t \in \{S_1, S_2, S_3, S_4\} 0 <= t <= k-1)$$

$$\begin{bmatrix} a_{11} & a_{12} & a_{13} & a_{14} \\ a_{21} & a_{22} & a_{23} & a_{24} \\ a_{31} & a_{32} & a_{33} & a_{34} \\ a_{41} & a_{42} & a_{43} & a_{44} \end{bmatrix} \begin{bmatrix} p_1(k) \\ p_2(k) \\ p_3(k) \\ p_4(k) \end{bmatrix} = \begin{bmatrix} p_1(k+1) \\ p_2(k+1) \\ p_3(k+1) \\ p_4(k+1) \end{bmatrix}$$

Linear map of matrix A can be expressed as. A is 4x4 so there should be 4 terms in the final math expression

$$A = \sum_{i=1}^{n} C_i \lambda_i \mathbf{v}_i$$

Where λ_i is the corresponding eigenvalue v_i is the corresponding eigenvector and C_i is the corresponding arbitrary constant

Thus at time step k the probabilty the channel is in the open state

$$P^c_{1,2,3,4}(k) = C_1\lambda_1^k\mathbf{v}^1 + C_2\lambda_2^k\mathbf{v}^2 + C_3\lambda_3^k\mathbf{v}^3 + C_4\lambda_4^k\mathbf{v}^4$$

II Simulating Markov chains and neural spiking

In [1]:
```
import matplotlib.pylab as plt   # That gives plotting, and the next line makes plots appear inl
%matplotlib inline
import numpy as np  # That gives numerical arrays and tools for manipulating them
import scipy.optimize as opt
import scipy.linalg as la

from scipy.optimize import curve_fit
```

In [2]:
```
# Initialize random number generator
rng = np.random.default_rng()
#Define Transition Matrices
A = np.array([[0.98, 0.10, 0],
             [0.02, 0.70, 0.05],
             [0, 0.20, 0.95]]) #Inward Channel

B = np.array([[0.90, 0.10, 0],
             [0.10, 0.60, 0.10],
             [0, 0.30, 0.90]]) #BOutward Channel
print(A)
print(B)
```

```
[[0.98 0.1  0.  ]
 [0.02 0.7  0.05]
 [0.   0.2  0.95]]
[[0.9 0.1 0. ]
 [0.1 0.6 0.1]
 [0.  0.3 0.9]]
```

In [3]:
```
def voltage_gate(Tmax, A, count, Direction):
    #matrix A
    states=np.zeros(Tmax,dtype=int)
    states[0]=0
    voltage=np.zeros(Tmax,dtype=int)
    voltage[0]=0
    plt.figure()
    for i in range(count):
        for t in np.arange(Tmax - 1):
            r = rng.uniform(0, 1) # draw random variable (uniformly distributed in 0,1)
            if states[t] == 0:
                if r < A[0, 0]: #transition 0 to 0
                    states[t + 1] = 0
                    voltage[t + 1] += 0
                else: #transition 0 to 1
                    states[t + 1] = 1

            elif states[t] == 1:
```

```
                if r < A[1, 1]: #transition 1 to 1.
                    states[t + 1] = 1
                elif A[1, 1] < r < A[1, 1] + A[0, 1]: #transition 1 to 0.
                    states[t + 1] = 0
                    #transition 1 to 1 < r < transition 1 to 1 + transition 1 to 0
                else: #transition 1 to 2
                    states[t + 1] = 2
                    if Direction == "Inward":
                        voltage[t + 1] += 1
                    else:
                        voltage[t + 1] -= 1

            elif states[t] == 2:
                if r < A[2, 2]: #transition 2 to 2
                    states[t + 1] = 2
                    if Direction == "Inward":
                        voltage[t + 1] += 1
                    else:
                        voltage[t + 1] -= 1
                else: #transition 2 to 1
                    states[t + 1] = 1
        #Plot of states
        #plt.plot(states)
        #plt.xlabel('state')
        #plt.ylabel('timestep')
        #plt.yticks([0, 1, 2])  # Limit y-axis to only show values 0, 1, 2
        #print(A)
    return states, voltage
```

Assume there are a total of $n_{inward} = 100$ inward channels, each evolving independently under a realization of the Markov kinetics above. If n_{inward} of these channels are in the open configuration at timestep t, then the total inward current is $+n_{inward}$

In [4]:
```
states_inward, voltage_inward = voltage_gate(Tmax=1000,A=A, count=100,Direction="Inward")
plt.figure()
plt.plot(voltage_inward, label="Inward Voltage", color="red")
plt.xlabel("Timestep")
plt.ylabel("Voltage")
plt.legend()
plt.title("Voltage over Time for Inward Channels")
plt.show()
```

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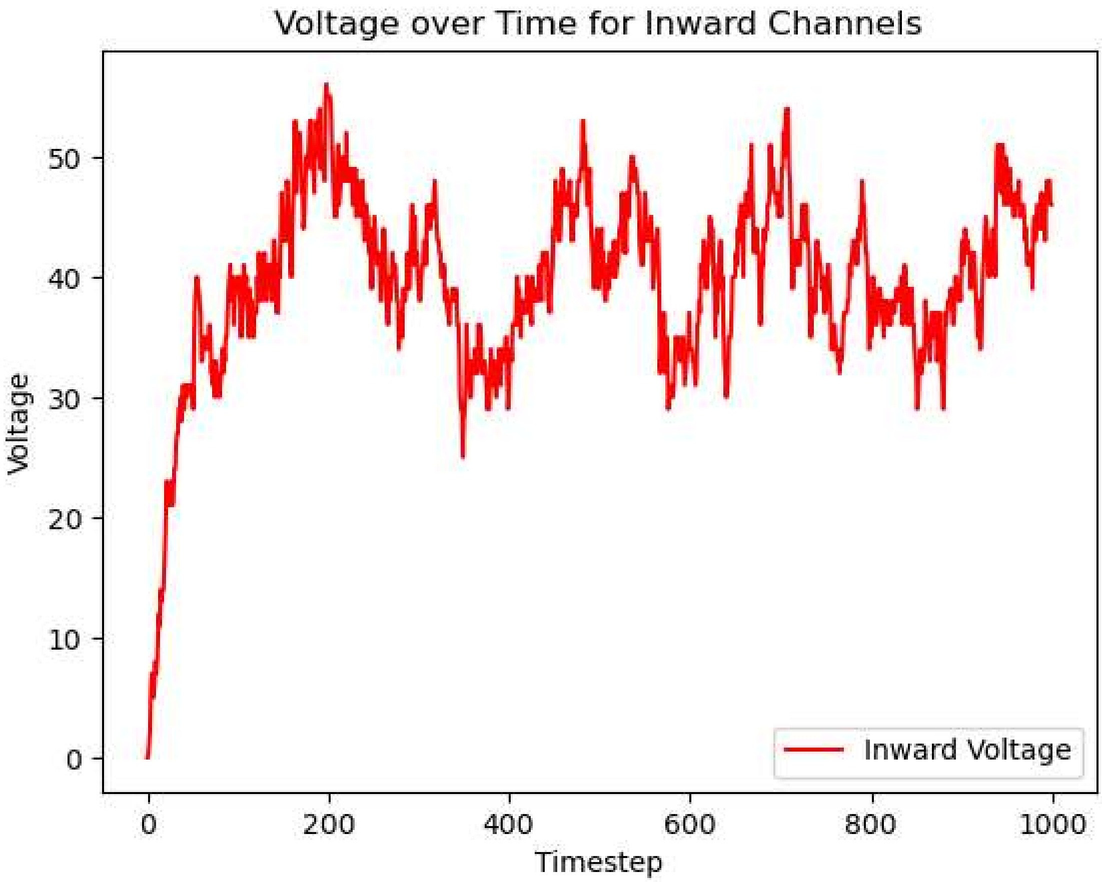
```



Assume there are a total of $N_{outward} = 50$ outward channels, each evolving independently under a realization of the Markov kinetics above. If $n_{outward}$ of these channels are in the open configuration at timestep t, then the total outward current is $-n_{outward}$ units.

In [5]:
```
states_outward, voltage_outward = voltage_gate(Tmax=1000,A=B, count=50,Direction="Outward")
plt.figure()
plt.plot(voltage_outward, label="Outward Voltage", color="blue")
plt.xlabel("Timestep")
plt.ylabel("Voltage")
plt.legend()
plt.title("Voltage over Time for Outward Channels")
plt.show()
```

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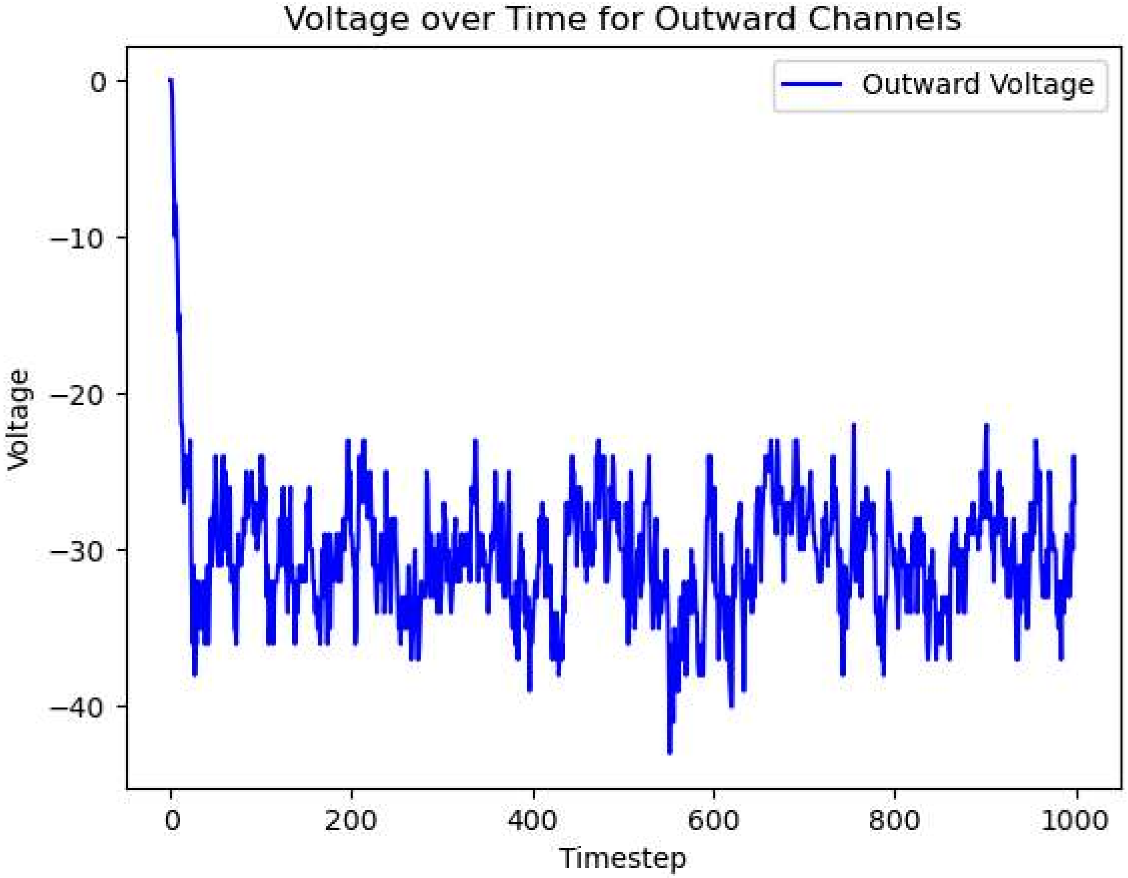
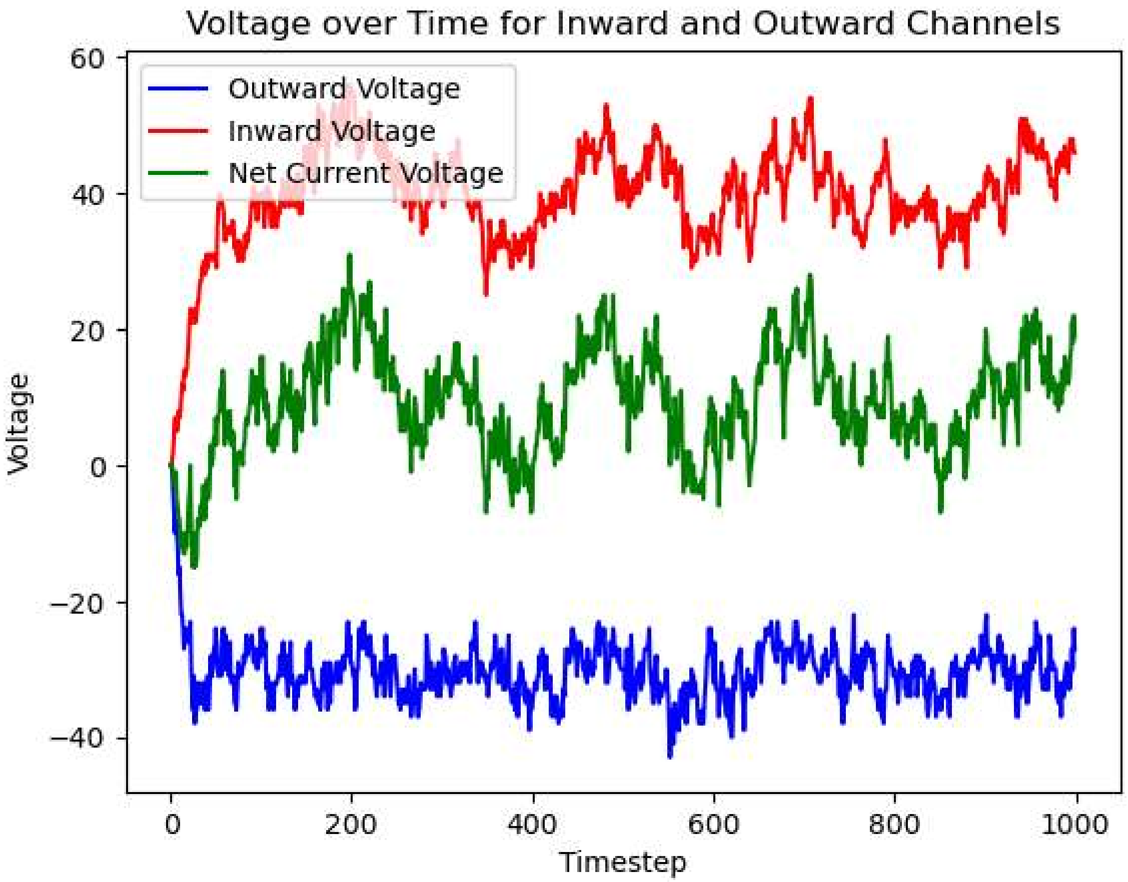


Thus, the net current into the cell at timestep t is $n_{inward} - n_{outward}$: the number of open inward channels minus the number of open outward channels.

In [6]:
```
net_current = voltage_inward + voltage_outward

#Plot of Net Current
plt.figure()
plt.plot(voltage_outward, label="Outward Voltage", color="blue")
plt.plot(voltage_inward, label="Inward Voltage", color="red")
plt.plot(net_current, label="Net Current Voltage", color="green")
plt.xlabel("Timestep")
plt.ylabel("Voltage")
plt.legend()
plt.title("Voltage over Time for Inward and Outward Channels")
plt.show()
```



In our model, the cell will produce an action potential (spike) in a given timestep if this net current is greater than a threshold value T. Assume that the channels have settled into equilibrium (i.e., that a time has passed that is large enough since a simulation was initialized). Plot the probability that the cell will produce a spike in a given timestep, as a function of the spiking threshold T.

There are at least two ways of doing this: (1) by computing the equilibrium state probabilities, and simulating many coin tossings, or (2) by computing the equilibrium state probabilities, and using the form of the binomial distribution.

In [7]:
```
# Define threshold range and Tmax
thresholds = np.arange(-20, 50, 1)
Tmax = 1000

# Define spike probability calculation function
def spike_probability(voltage, thresholds):
    spike_probs = []
    for T in thresholds:
        spikes = np.sum(voltage >= T)  # Count timesteps where voltage >= T
        spike_prob = spikes / len(voltage)  # Fraction of timesteps with spikes
        spike_probs.append(spike_prob)
    return spike_probs

# Create subplots with a 2x3 grid
fig, axes = plt.subplots(2, 3, figsize=(18, 10))  # Adjust figsize as needed
counts = [10, 100, 1000]

for i, count in enumerate(counts):
    # Generate voltage data
    states_inward, voltage_inward = voltage_gate(Tmax=Tmax, A=A, count=count, Direction="Inward"
    states_outward, voltage_outward = voltage_gate(Tmax=Tmax, A=B, count=count // 2, Direction="(

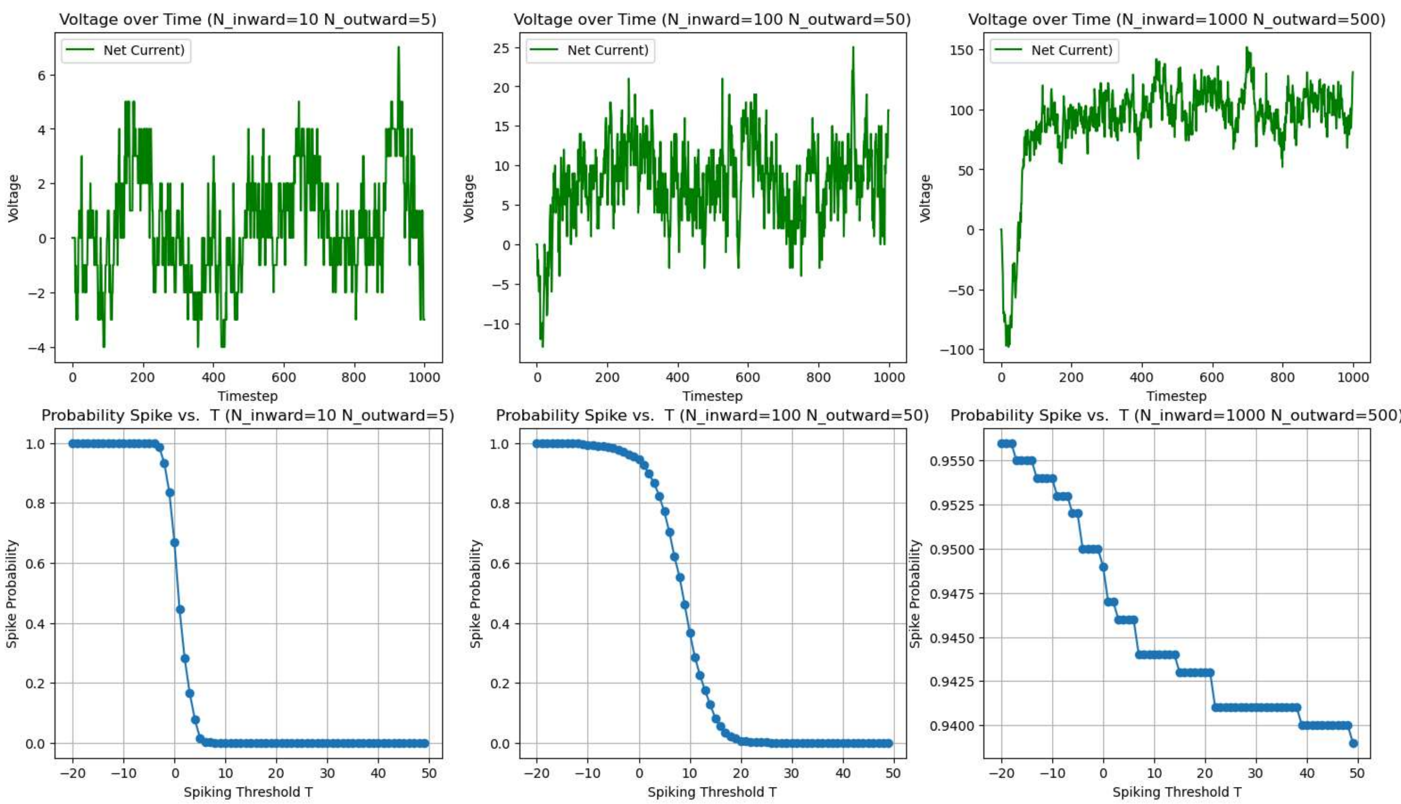
    # Calculate net current and spike probabilities
```

```python
    net_current = voltage_inward + voltage_outward
    spike_probs = spike_probability(net_current, thresholds)

    # Plot net current voltage over time
    ax1 = axes[0, i]  # First row
    ax1.plot(net_current, label=f"Net Current)", color="green")
    ax1.set_xlabel("Timestep")
    ax1.set_ylabel("Voltage")
    ax1.legend()
    ax1.set_title(f"Voltage over Time (N_inward={count} N_outward={count//2})")

    # Plot spike probability vs. threshold
    ax2 = axes[1, i]  # Second row
    ax2.plot(thresholds, spike_probs, marker='o', linestyle='-')
    ax2.set_xlabel("Spiking Threshold T")
    ax2.set_ylabel("Spike Probability")
    ax2.set_title(f"Probability Spike vs.  T (N_inward={count} N_outward={count//2})")
    ax2.grid(True)

# Adjust layout and display
plt.tight_layout()
plt.show()
```

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```

(2) by computing the equilibrium state probabilities, and using the form of the binomial distribution.

Write a few sentences reporting on any qualitative changes that you observe.

In [8]:
```python
# At longer time the average net current is more settled on one value. At shorter Time max there
# The more outward and inward channels there are the larger the magnitude of the net current.
```

```
# When there are double the amount of inward channels compared to outward channels there is a mor
# It appears the et current is
# The longer the timestep the more smooth the function of the thresholds is.
# The threshold proabbiility shape is relativiely constant
# There is no major difference between the amounts on the size of the net current.
# The net membrane can be either positive or negative
```