Array Recording Simulation and Neuron Spike Clustering

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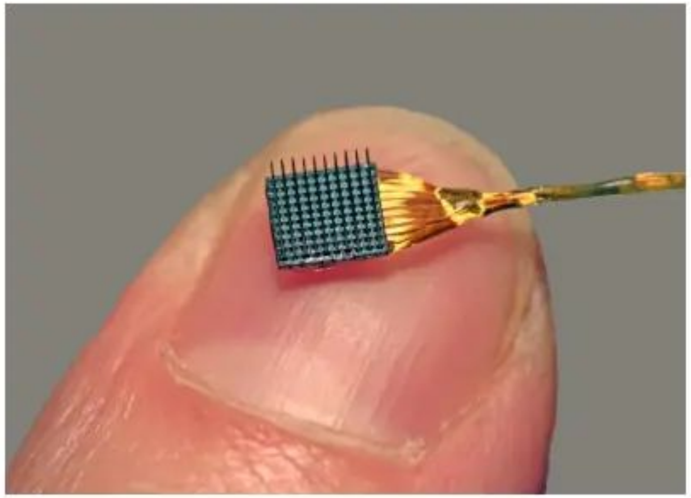
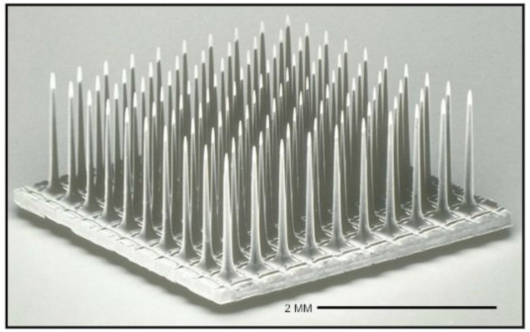
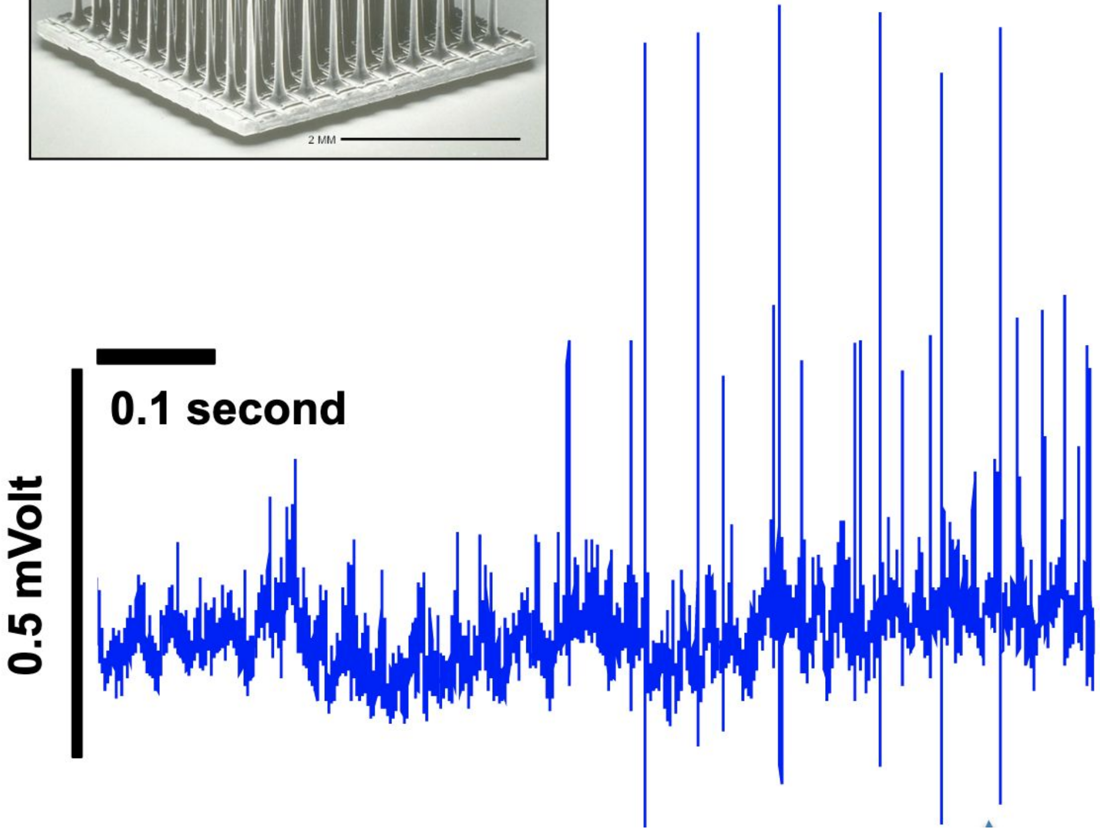
INTRODUCTION

Array Recordings,
Aims, and Hypothesis

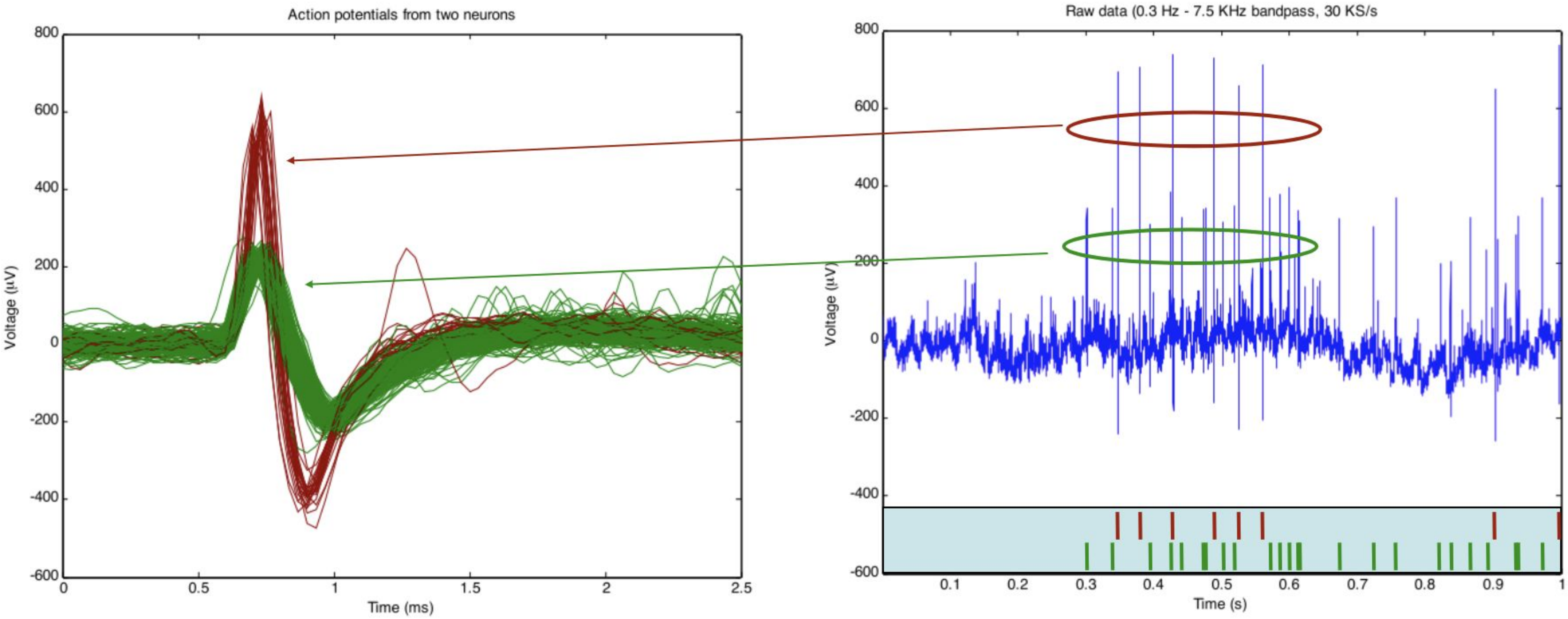
Background







Aims and Hypothesis



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METHODS

Array Recording Simulation: 2 Methods

Method 1: Simulating Extracellular Recording of 2 Hodgkin-Huxley Neurons

$$\frac{dm}{dt} = \alpha_m (1-m) - \beta_m m$$

$$\frac{dh}{dt} = \alpha_h (1-h) - \beta_h h$$

$$\frac{dn}{dt} = \alpha_n (1-n) - \beta_n n$$

$$C_m \frac{\partial V_m}{\partial dt} = G_L (E_L - V_m) + G_{Na} m^3 h (E_{Na} - V_m) + G_K n^4 (E_K - V_m) + I_{app}$$

$$V_m(i) = V_m(i-1) + \partial V_m \partial t + NOISE$$

Method 2: Simulating Extracellular Recording of 2 Connors-Stevens Neurons

$$\frac{dm}{dt} = \alpha_m (1-m) - \beta_m m$$

$$\frac{dh}{dt} = \alpha_h (1-h) - \beta_h h$$

$$\frac{dn}{dt} = \alpha_n (1-n) - \beta_n n$$

$$\frac{da}{dt} = \frac{a_\infty - a}{\tau_a}$$

$$\frac{db}{dt} = \frac{b_\infty - b}{\tau_b}$$

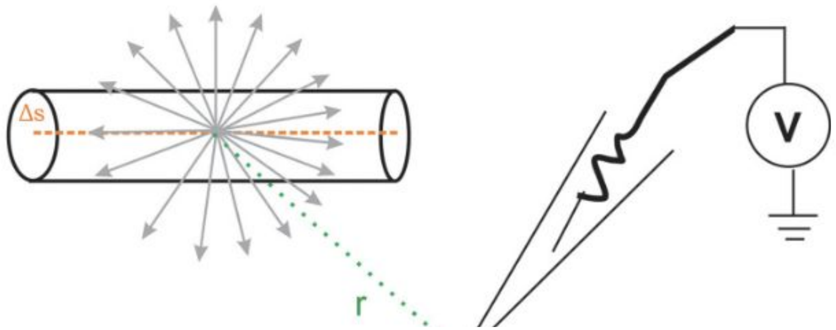
$$C_m \frac{dV_m}{dt} = G_L (E_L - V_m) + G_{Na}^{(max)} m^3 h (E_{Na} - V_m) + G_K^{(max)} n^4 (E_K - V_m) + G_A^{(max)} a^3 b (E_A - V_m) + I_{app}$$

$$V_m(i) = V_m(i-1) + \partial V_m \partial t + NOISE$$

Point Source Approximation to Generate Voltage Traces

GOAL: Simulate the recorded activity of two neurons using PSA to generate individual voltage traces and sum them to make the final simulated recording

Point Source Approximation



$$I_{transmemberane} = I_{ionic} + c_m \frac{\partial V_m}{\partial t}$$

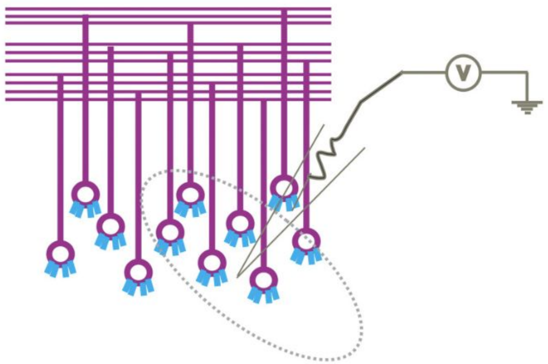
$$\sigma \nabla \Phi = J_m$$

Φ = approximated extracellular potential
σ = conductance of extracellular medium
r = distance between neuron point source and recording electrode

This approximation is based on Ohm's Law

$$\Phi_{LFP} = \sum_{i=1}^{n\_sources} \frac{I_i}{4\pi\sigma r_i}$$

Here, Φ_{LFP} is the summed approximation of extracellular potentials from point sources, to be clear we are not generating LFP, but rather using a method to generate LFP to instead simulate the activity of two spiking neurons



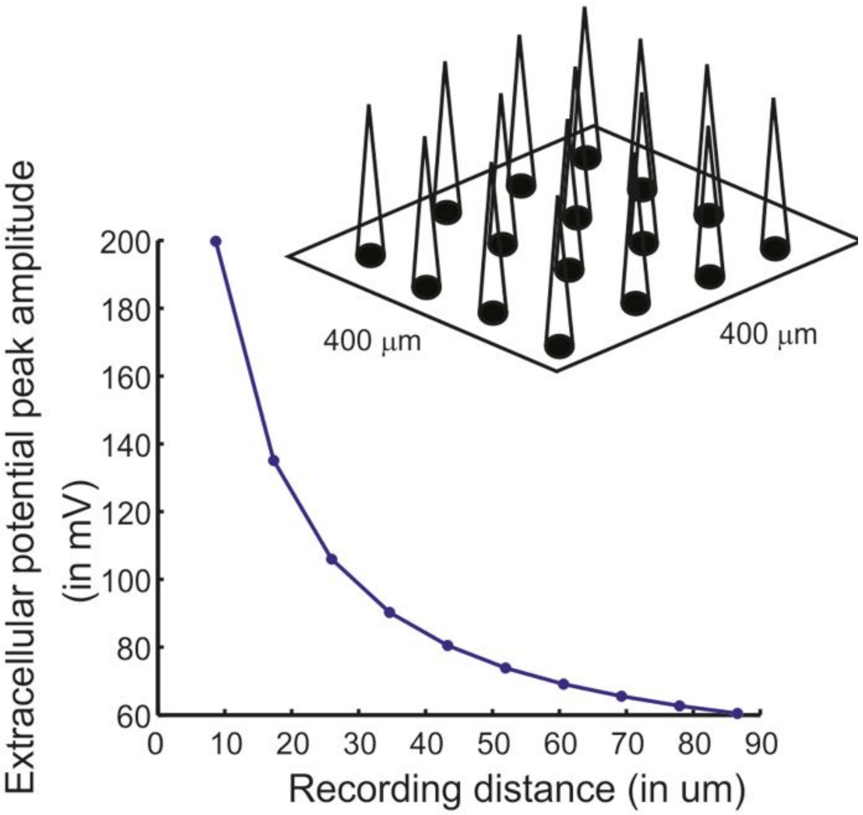
$$J = \frac{I}{A}$$

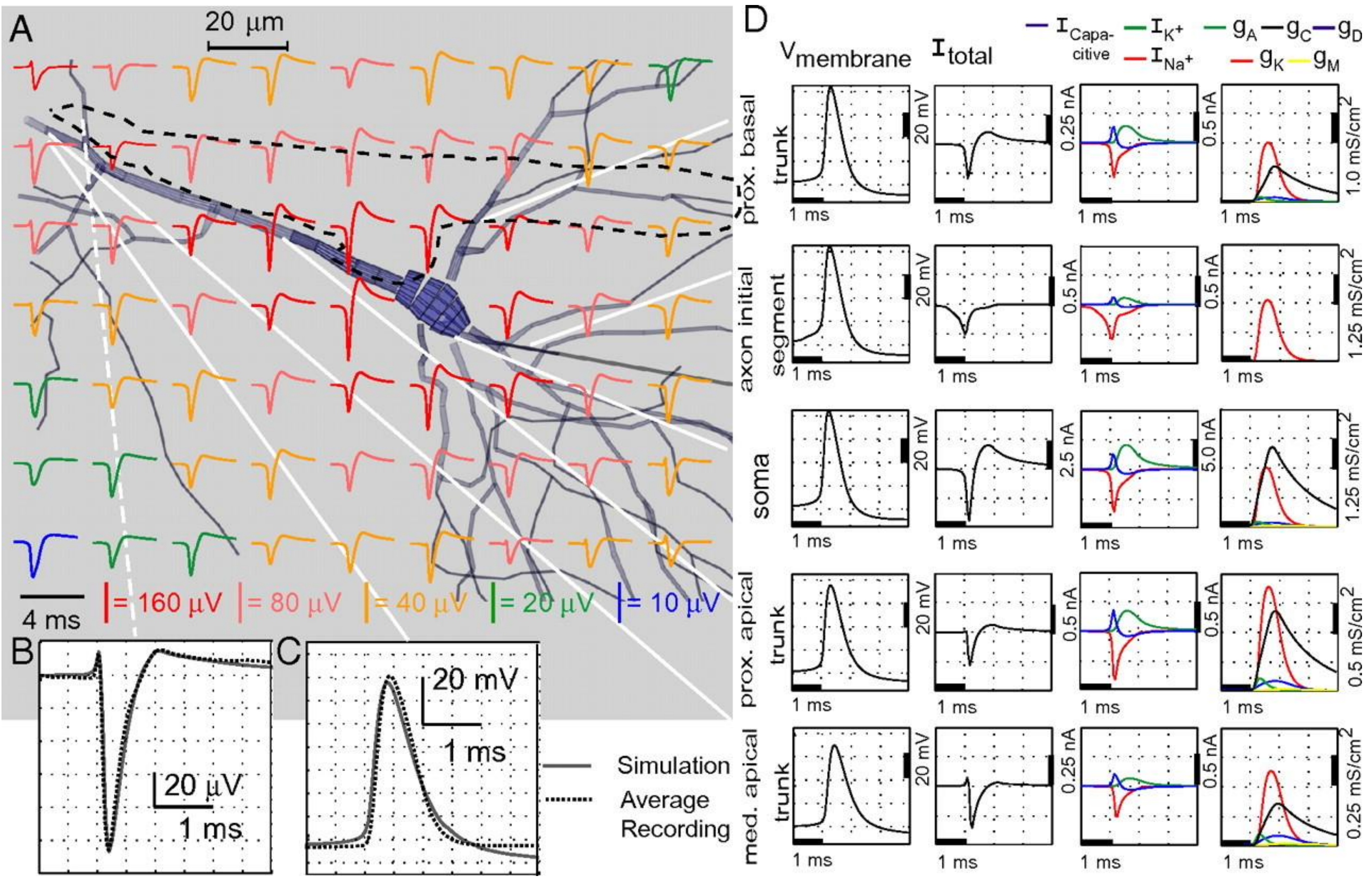
$$V = IR$$

$$\Phi = \frac{I}{4\pi\sigma r}$$

$$J = \sigma E$$

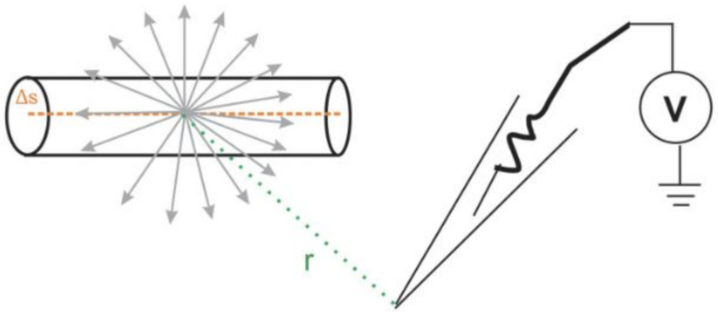
Point Source Approximation





Simulating 2 Neurons Using Point Source Approximation to Calculate Extracellular Potential

Point Source Approximation



$$\Phi_{LFP} = \sum_{i=1}^{n\_sources} \frac{I_i}{4\pi\sigma r_i}$$

$$\Phi = \frac{I}{4\pi\sigma r}$$

$$V = IR$$

$$C_m \frac{\partial V_m}{\partial dt} = G_L\left(E_L - V_m\right) + G_{Na} m^3 h\left(E_{Na} - V_m\right) + G_K n^4\left(E_K - V_m\right) + I_{app}$$

$$C_m \frac{dV_m}{dt} = G_L\left(E_L - V_m\right) + G_{Na}^{(max)} m^3 h\left(E_{Na} - V_m\right) + G_K^{(max)} n^4\left(E_K - V_m\right) + G_A^{(max)} a^3 b\left(E_A - V_m\right) + I_{app}$$

$$V_m(i) = V_m(i-1) + \partial V_m \partial t + NOISE$$

Key assumptions:

1. Homogenous extracellular medium
2. Purely ohmic conductance through the medium
3. Current dissipates linearly as a function of r
4. Treats I as a POINT SOURCE, and calculations can be done on a simple sum of all currents across the neuron acting as a point source
5. A linear relationship is assumed between the transmembrane current density and the electric potential at a distance r. (Ohm's Law)

The Model: PSA1(HH) and PSA2 (CS)

```
function [V] = PSA2(I,r,noise)
% Point Source Approximation based on Connors Stevens Model
% inputs are I in nA and r (distance from recroding electode) in
% and noise

% Connors Stevens Parameters
Gmax_Na=12e-6;        % maximum sodium conductance (S)
Gmax_K=3.6e-6;        % maximum delayed rectifier conductance (S)
G_L=30e-9;            % leak conductance (S)
E_Na=45e-3;           % sodium reversal potential (V)
E_K=-82e-3;           % potassium reversal potential (V)
E_L=-60e-3;           % leak reversal potential (V)
Cm=100e-12;           % membrance capaictance (F)

Gmax_A=25e-9;           % A-current conductance (S)
E_A=-70e-3;             % A-current reversal potential (V)

% Initialize Vectors
dt=0.00002;             % time step (s)
tmax=1.1;               % max time value (s)
tvect=0:dt:tmax;        % time vector (s)
Vm=zeros(size(tvect)); % membrane potential Vm vector
Vm(1)=-0.065;           % set initial condition (V)
m=zeros(size(tvect));  % gating variable m vector
m(1)=0.05;              % set initial condition
h=zeros(size(tvect));  % gating variable h vector
h(1)=0.5;               % set initial condition
n=zeros(size(tvect));  % gating variable n vector
n(1)=0.35;              % set initial condition
a=zeros(size(tvect));  % gating variable a vector
a(1)=0.05;              % set initial condition
b=zeros(size(tvect));  % gating variable b vector
b(1)=0.05;              % set initial condition

%PSA Values
sigma = 0.43;         % Siemens / m^2 medium conductivity
R = r * 10^-7;        % in meters (one micron = 1e-6 meters)
w = noise;            % noise scalar
```

```
for i=2:length(tvect)              % integrate over time

    dVmdt(i-1)=(1/Cm) * (G_L*(E_L-Vm(i-1)) + Gmax_Na*((m(i-1))^3)*h(i-1)*(E_Na-Vm(i-1)) + Gmax_K*((n(i-1))^4)*(E_K-Vm(i-1)) + Gmax_A*((a(i-1))^3)*b(i-1)*(E_A-Vm(i-1)) + Iapp_vect(i-1));   %
    Vm(i)=Vm(i-1)+dVmdt(i-1)*dt + randn()*w;       % update Vm

    dmdt=(((10^5)*(-Vm(i-1)-0.045))/(exp(100*(-Vm(i-1)-0.045))-1))*(1-m(i-1)) - (4*(10^3)*exp((-Vm(i-1)-0.070)/0.018))*m(i-1);   % define m rate of change
    m(i)=m(i-1)+dmdt*dt;           % update m

    dhdt=(70*exp(50*(-Vm(i-1)-0.070)))*(1-h(i-1)) - ((10^3)/(1+exp(100*(-Vm(i-1)-0.040))))*h(i-1);   % define h rate of change
    h(i)=h(i-1)+dhdt*dt;           % update h

    dndt=(((10^4)*(-Vm(i-1)-0.060))/(exp(100*(-Vm(i-1)-0.060))-1))*(1-n(i-1)) - (125*exp((-Vm(i-1)-0.070)/0.08))*n(i-1);   % define n rate of change
    n(i)=n(i-1)+dndt*dt;           % update n

    dadt=((0.3)-a(i-1))/0.0005;   % define h rate of change
    a(i)=a(i-1)+dadt*dt;           % update a

    dbdt=((0.2)-b(i-1))/0.0005;   % define n rate of change
    b(i)=b(i-1)+dbdt*dt;           % update b

    Iionic(i-1) = (G_L*(E_L-Vm(i-1)) + Gmax_Na*((m(i-1))^3)*h(i-1)*(E_Na-Vm(i-1)) + Gmax_K*((n(i-1))^4)*(E_K-Vm(i-1)) + Gmax_A*((a(i-1))^3)*b(i-1)*(E_A-Vm(i-1)));
    Im(i-1) = (dVmdt(i-1) * Cm )+ Iionic(i-1);    % calculate Im
    theta(i-1) = Im(i-1)/(4*pi*sigma*R); %calculate PSA potential

end
```

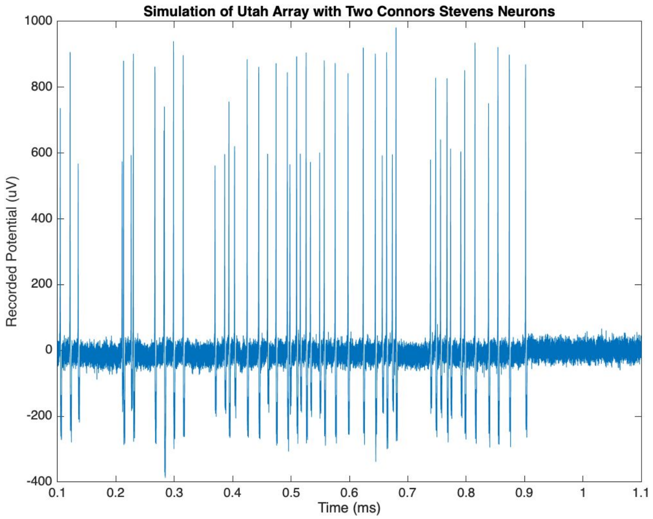
Features of the functions:

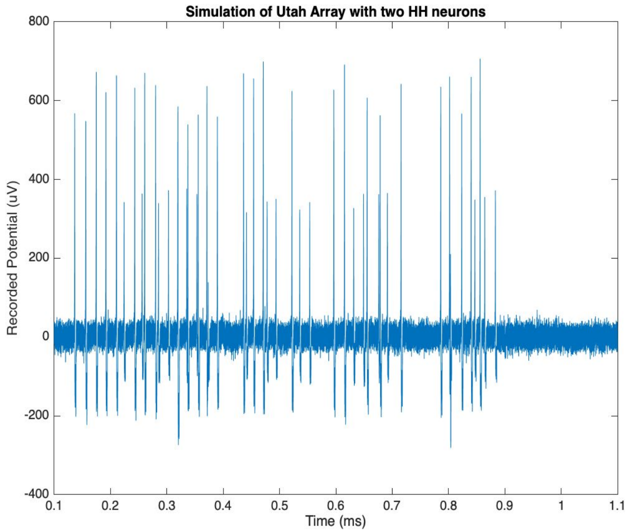
1. PSA1 runs point source approximation based on Hodgkin Huxley model
2. PSA2 runs point source approximation based on Connors Stevens model

The Model: PSA1 and PSA2

```
% SIMULATE UTAH RECORDING OF TWO CONNORS STEVENS NEURONS

clear

% Time Vector

dt=0.00002;           % time step (s)
tmax=1.1;             % max time value 1 second (s)
tvect= 0:dt:tmax;     % time vector, a second

% LFP Noise Vector
hi = 16;               % noise scalar
LFP_vec = randn(1, length(tvect)); % empty LFP vector
LFP_vec = LFP_vec*hi;  % scaled LFP vector

V1 = PSA2(5,10,0.0002);   % run PSA2 (Connors Stevens) simulation for a neuron 7 microns away with a 5 nA applied current with noise.
V2 = PSA2(5,15,0.0002);  % run PSA2 (Connors Stevens) simulation for a neuron 15 microns away with a 5 nA applied current with noise.

V3 = V1+V2;                % Sum the voltage trace outputs

V3 = V3*100 + LFP_vec;     % Add LFP noise, final trace

start_time = 0.1;  % Start time to remove (in seconds)
start_index = find(tvect >= start_time, 1);  % Find the index corresponding to the start time
V3 = V3(start_index:end);
tvect = tvect(start_index:end);  % Remove the time values before the start index

%Plot

figure;
plot(tvect,V3);
title('Simulation of Utah Array with Two Connors Stevens Neurons')
xlabel('Time (ms)');
ylabel('Recorded Potential (uV)');
```

```
% SIMULATE UTAH RECORDING OF TWO HH NEURONS

% Time Vector

dt=0.00002;           % time step (s)
tmax=1.1;             % max time value 1 second (s)
tvect= 0:dt:tmax;     % time vector, a second

% LFP Noise Vector
hi = 16;
LFP_vec = randn(1, length(tvect));
LFP_vec = LFP_vec*hi;


T1 = PSA1(5,7,0.0002);  % Simulate the PSA of a neuron with applied current of 5 nA, 7 microns away from recording electrode, with added noise
T2 = PSA1(5,13,0.0002); % Simulate the PSA of a neuron with applied current of 5 nA, 13 microns away from recording electode, with added noise
T3 = T1+T2;             % Sum the voltage trace outputs

T3 = T3*100 + LFP_vec;  % Add LFP noise, final trace

% This is done to remove artifacts present at the time of the start of the
% pulse

start_time = 0.1;  % Start time to remove (in seconds)
start_index = find(tvect >= start_time, 1);  % Find the index corresponding to the start time
T3 = T3(start_index:end);
tvect = tvect(start_index:end);              % Remove the time values before the start index

%Plot
figure;
plot(tvect,T3);
title('Simulation of Utah Array with two HH neurons')
xlabel('Time (ms)');
ylabel('Recorded Potential (uV)');
hold off
```





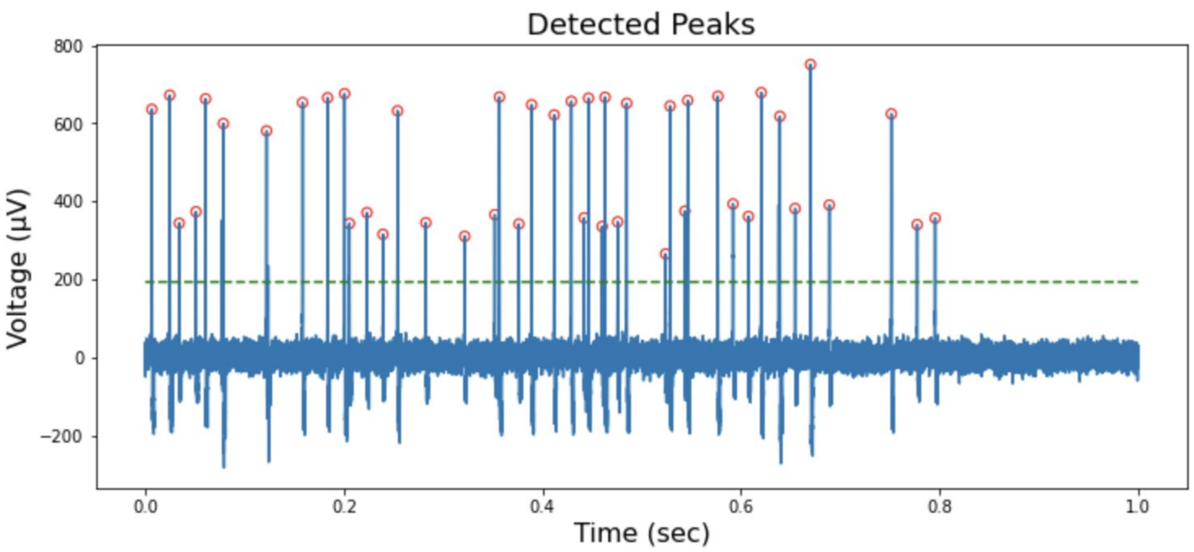
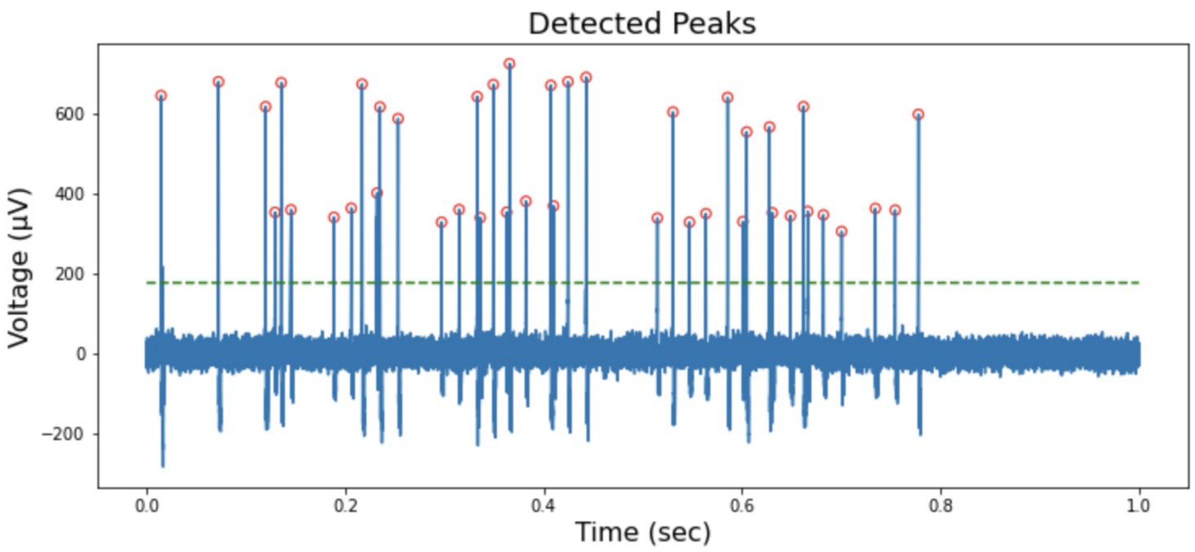
Features of the functions:

1. Initialize Parameters
2. Generate Step Pulse
3. Forward Euler's Method
4. Calculate PSA
5. Plot Traces

METHODS

Neuron Spike Clustering

Spike Detection: Height Threshold of 3*RMS and Time Threshold of 2 ms

Hodgkin-Huxley Model	Connor-Stevens Model
	

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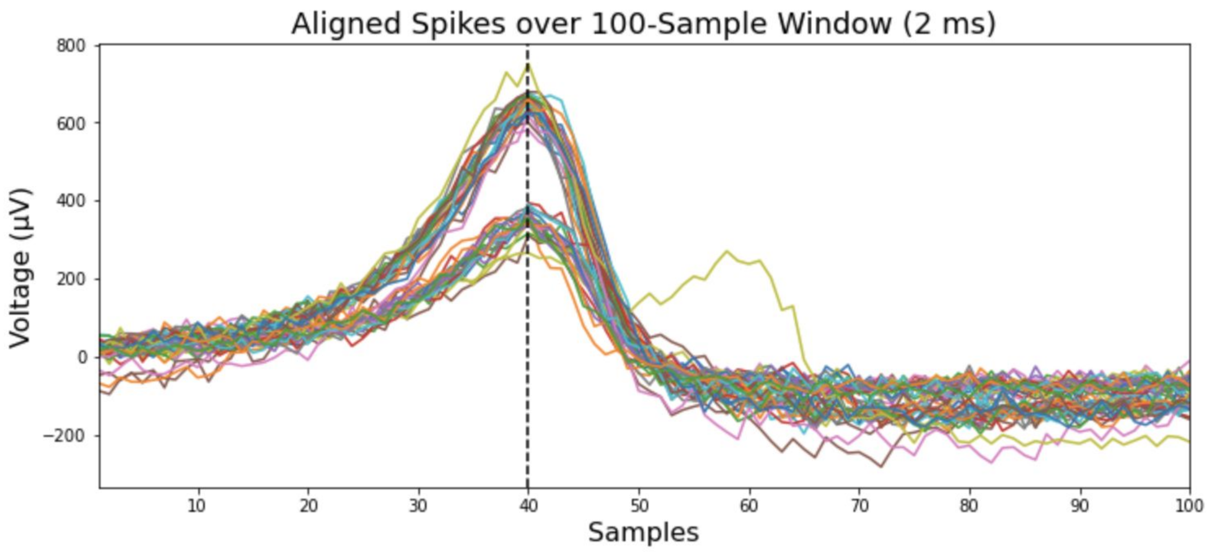
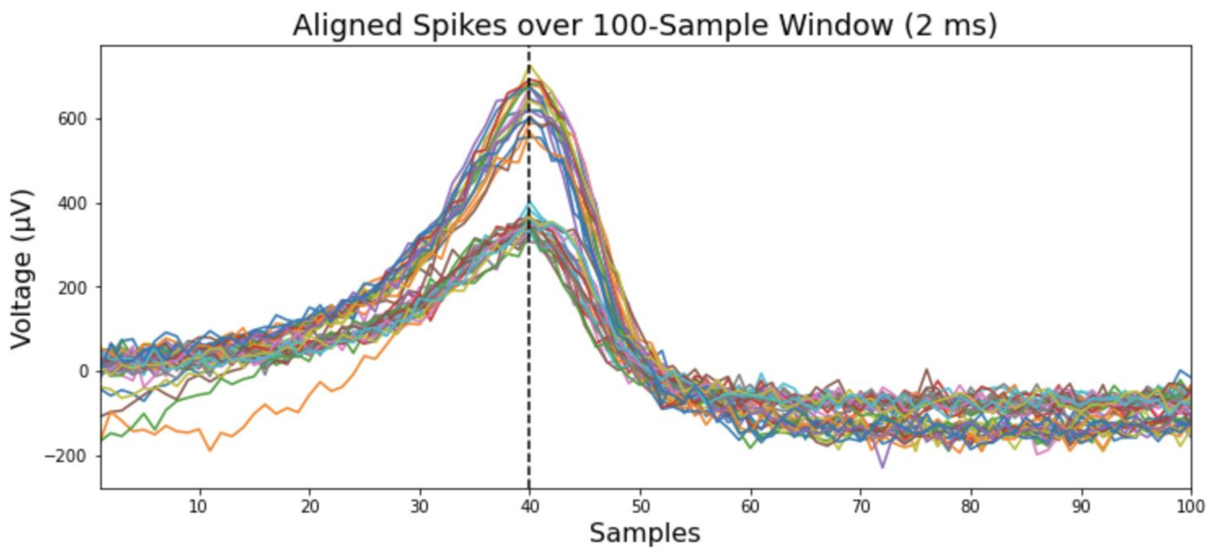
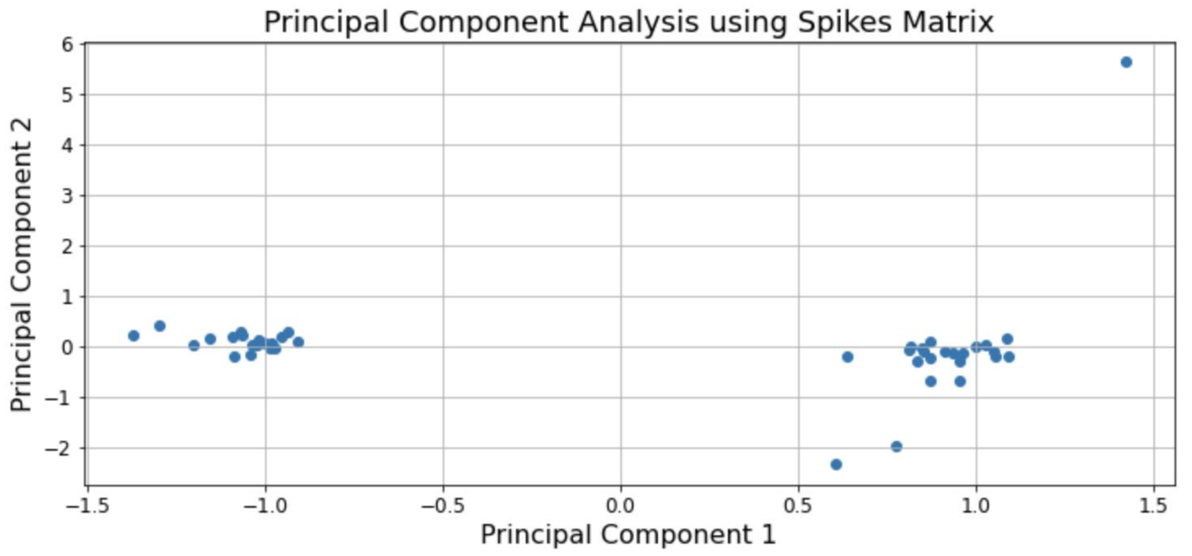
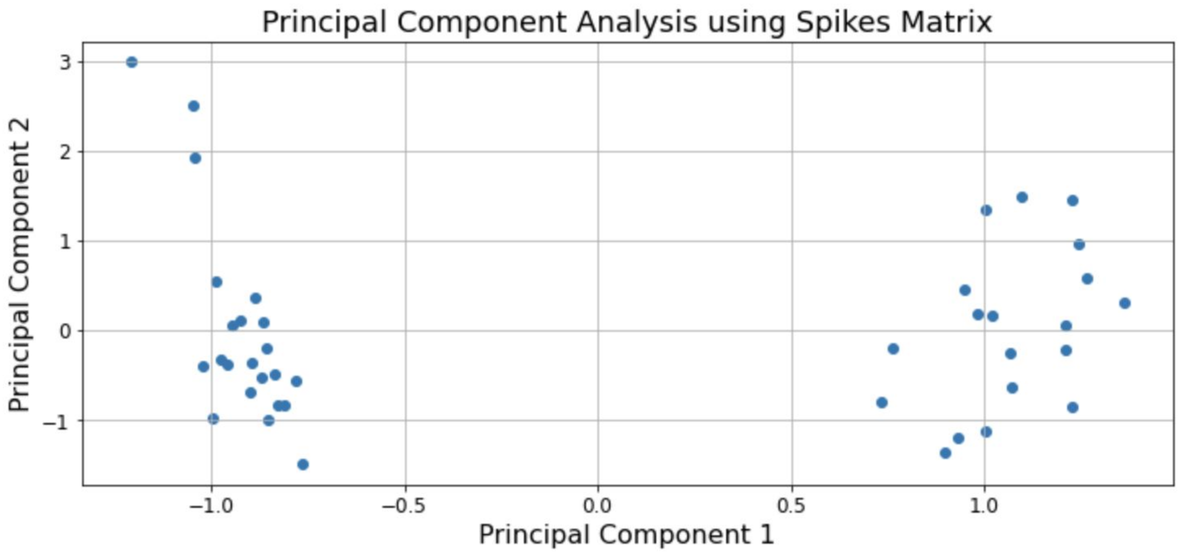
Spike Alignment: 2-ms Segments with Centered around the Detected Peak

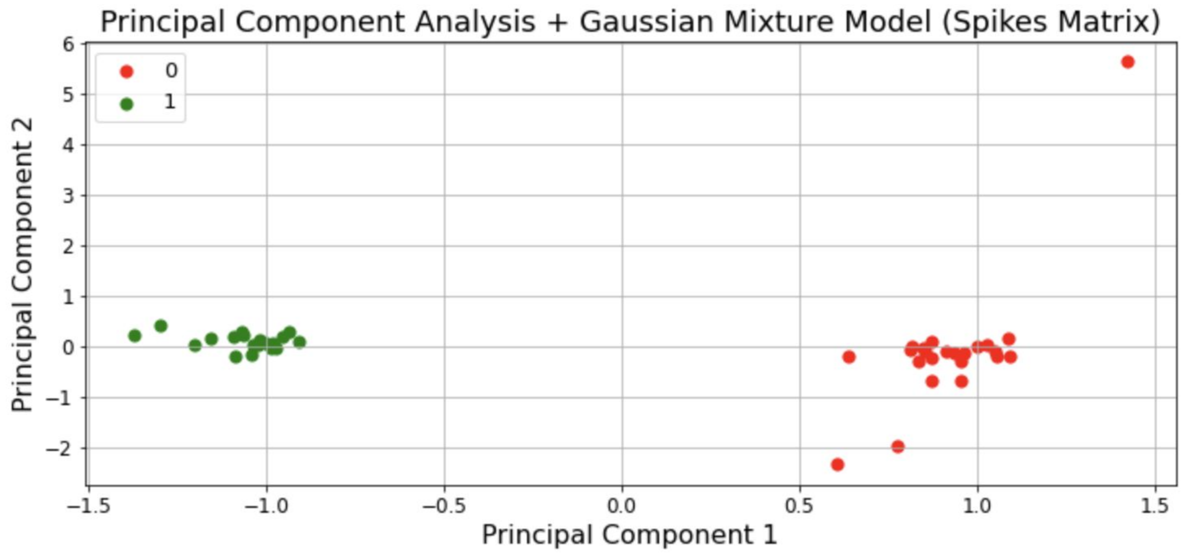
Hodgkin-Huxley Model	Connor-Stevens Model
	

Feature Extraction: 2 First Principal Components

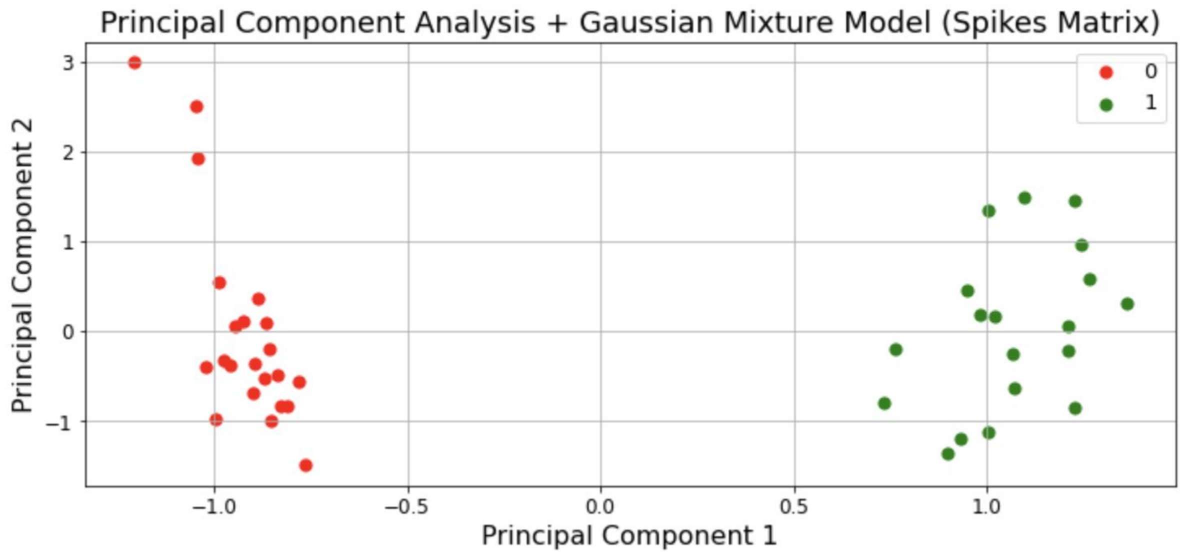
Hodgkin-Huxley Model	Connor-Stevens Model
	

Spike Classification: Gaussian Mixture Model (GMM)

Hodgkin-Huxley Model



Connor-Stevens Model



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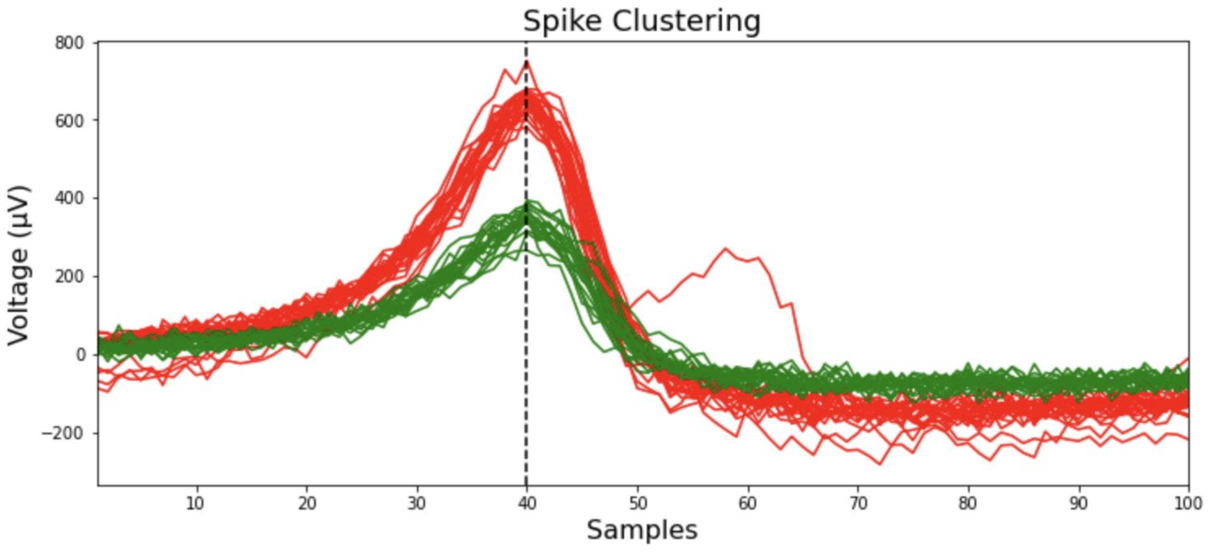
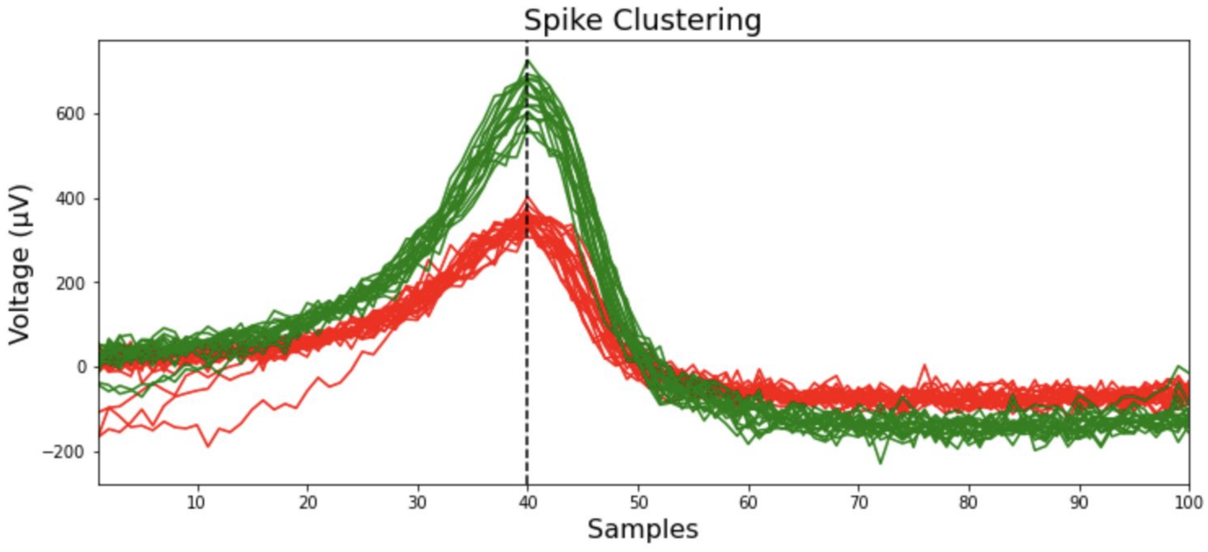
Spike Clustering: 2-ms Spike Segments with GMM Labels

Hodgkin-Huxley Model	Connor-Stevens Model
	

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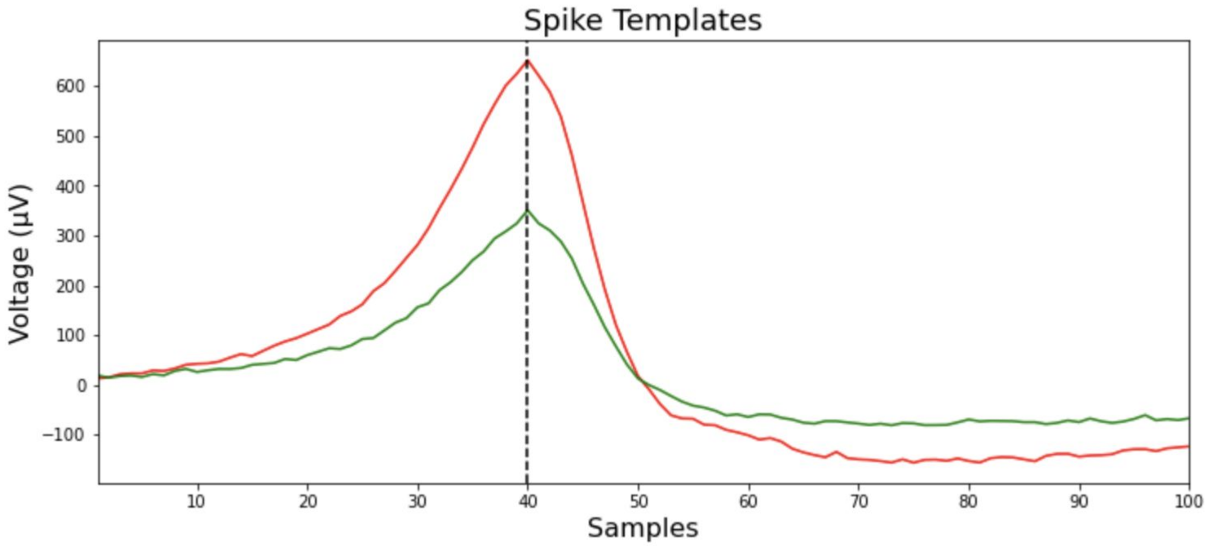
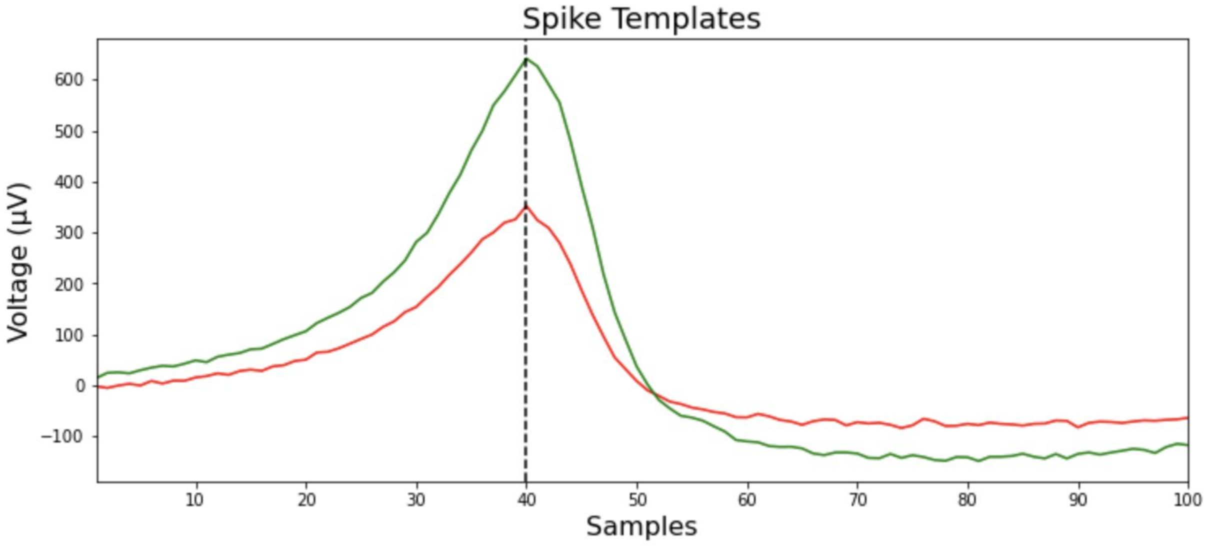
Spike Templates: 2-ms Mean of GMM Labeled Spike Segments

Hodgkin-Huxley Model	Connor-Stevens Model
	

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Flowchart of Neuron Spike Sorting Model

Simulated Utah Array Recording

↓

Spike Detection:
3RMS Height Threshold and
2-ms Time Threshold

↓

Spike Alignment: 2-ms Segments
Centered around
the Detected Peak

↓

Feature Extraction: 2 Principal
Components using Principal
Component Analysis

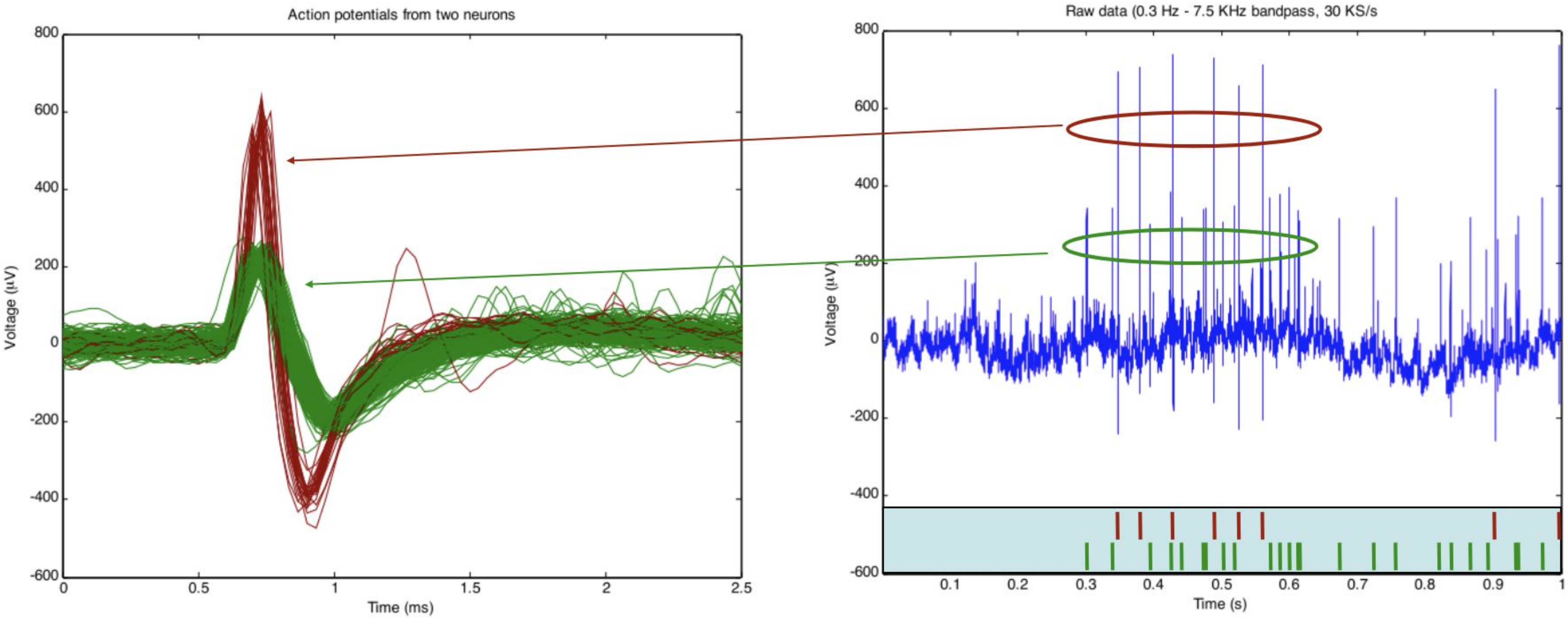
↓

Spike Clustering: Gaussian
Mixture Model

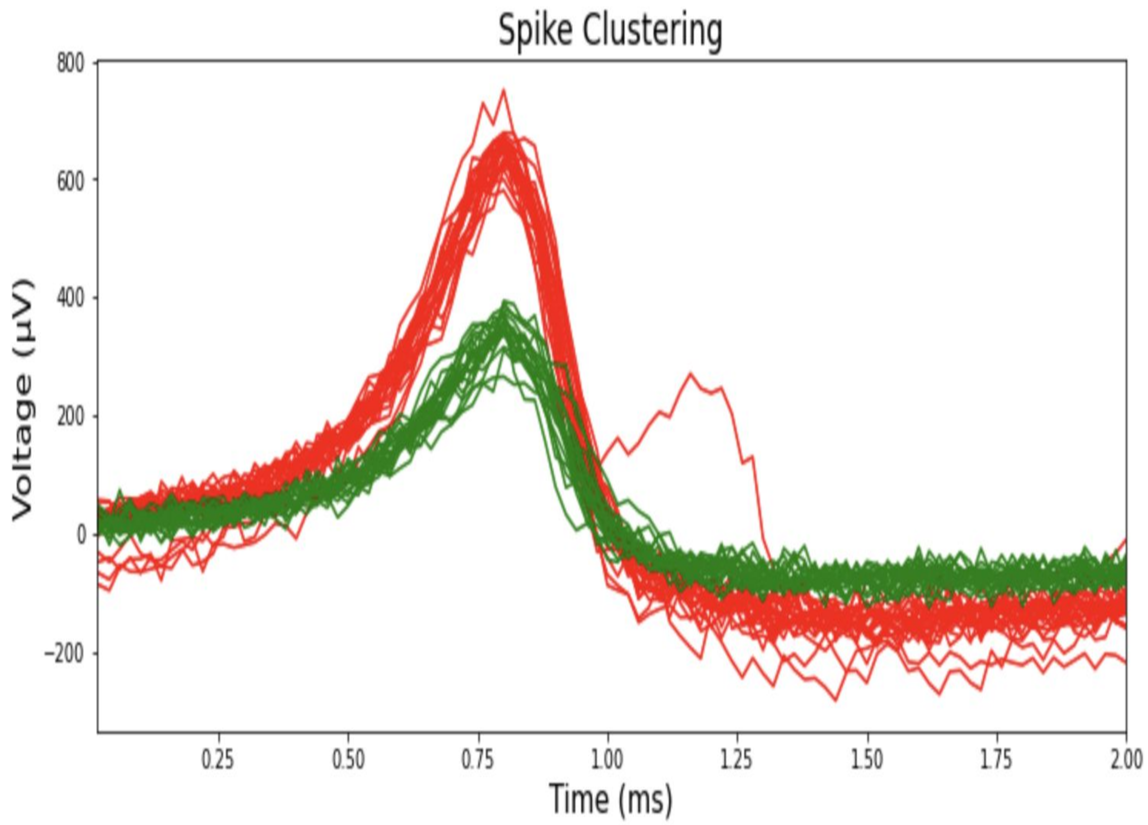
RESULTS

Utah Array Recordings

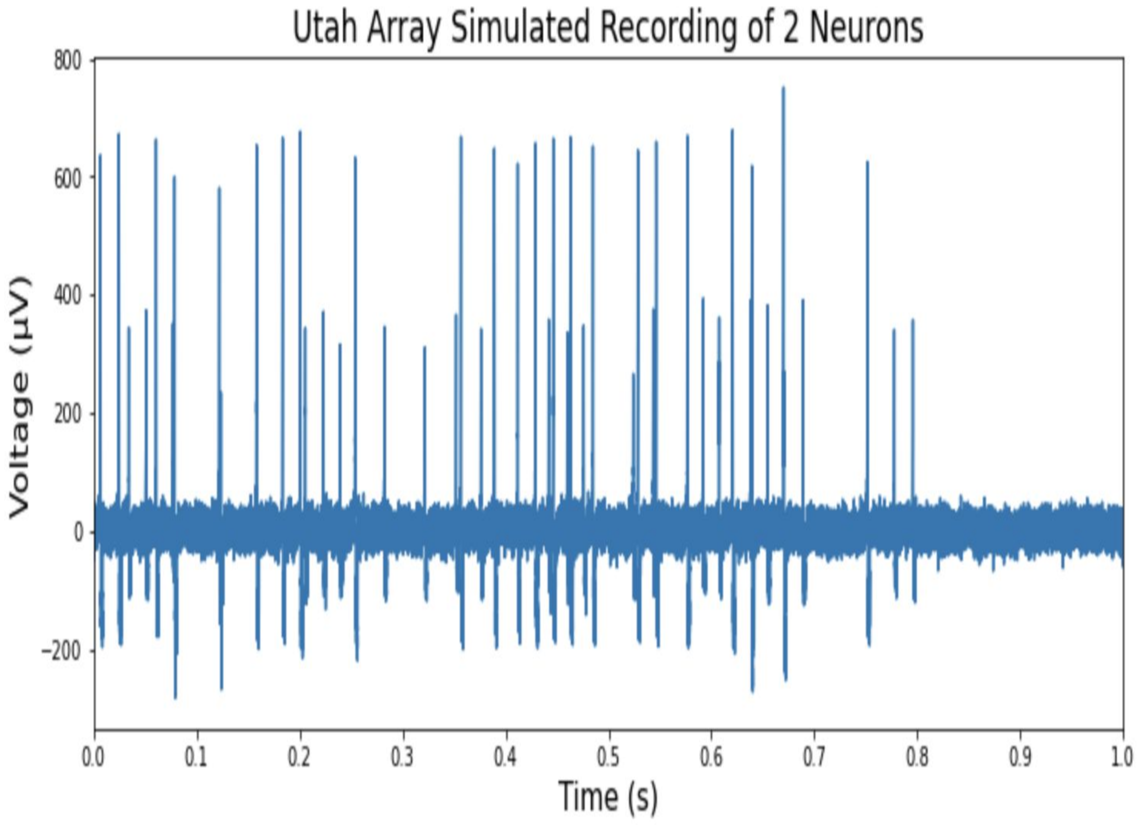
Aim: Replicate this



Look at this!



Spike Clustering
800
600
400
200
0
−200
Voltage (µV)
0.25
0.50
0.75
1.00
1.25
1.50
1.75
2.00
Time (ms)



Utah Array Simulated Recording of 2 Neurons
800
600
400
200
0
−200
Voltage (µV)
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
Time (s)

CONCLUSION

It is possible!

To make simulation even more realistic, we can add several neurons at a very large distance from the electrode. The goal is to make their action potentials small enough that they would only contribute to the LFP baseline to make it variable rather than constant at 0.

References

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