Integrate and Fire Model

The Integrate-and-fire model of neuron's firing consists of of the following equation for the membrane potential (in dimensionless units):

$$\begin{aligned} \tau \frac{dV}{dt} &= -V + I_e \\ V(t_{spike}^{-}) &= 1 \\ V(t_{spike}^{+}) &= 0 \end{aligned} \tag{1}$$

However, the model ignores two important biological observations. First, the action potential has a finite temporal width. Second, after firing an action potential, a neuron is less likely to fire an action potential in a short refractory period, contributed by the large persistent voltage-gated potassium current. To incorporate these ingredients into the model, Here we consider two different modifications.

1. We assume that after a spike the neuron's potential is strongly refractory, namely it is unable to respond to an external input for a period of time, τ_r where τ_r is of the order of a few milliseconds. Mathematically, this assumption can be written as,

$$V(t) = 0, t_{spike} < t < t_{spike} + \tau_r. \tag{2}$$

(a) Please compute the $f - I_e$ curve (firing frequency vs applied current) of this neuron. Analyze its behavior for large I_e, and compare it to the behavior at large I of the normal I-F neuron (i.e., without refractoriness). *Hint*: Use Taylor expansion in $1/I_e$. Additionally, explore the effect of τ_r, by plotting the two curves (with and without refractoriness using the following parameters: $\tau = 20$ ms $\tau_r = 2$ ms.

① 无不应期时：

求解微分方程：$\tau \frac{dV}{dt} = -V + I_e$

$$\frac{dV}{dt} = \frac{1}{\tau}(I_e - V)$$

$$\frac{dV}{I_e - V} = \frac{1}{\tau} dt$$

$$\int \frac{1}{I_e - V} dV = \int \frac{1}{\tau} dt$$

$$-\ln|I_e - V| = \frac{1}{\tau}(t + C)$$

$$|I_e - V| = e^{-\frac{t+C}{\tau}}$$

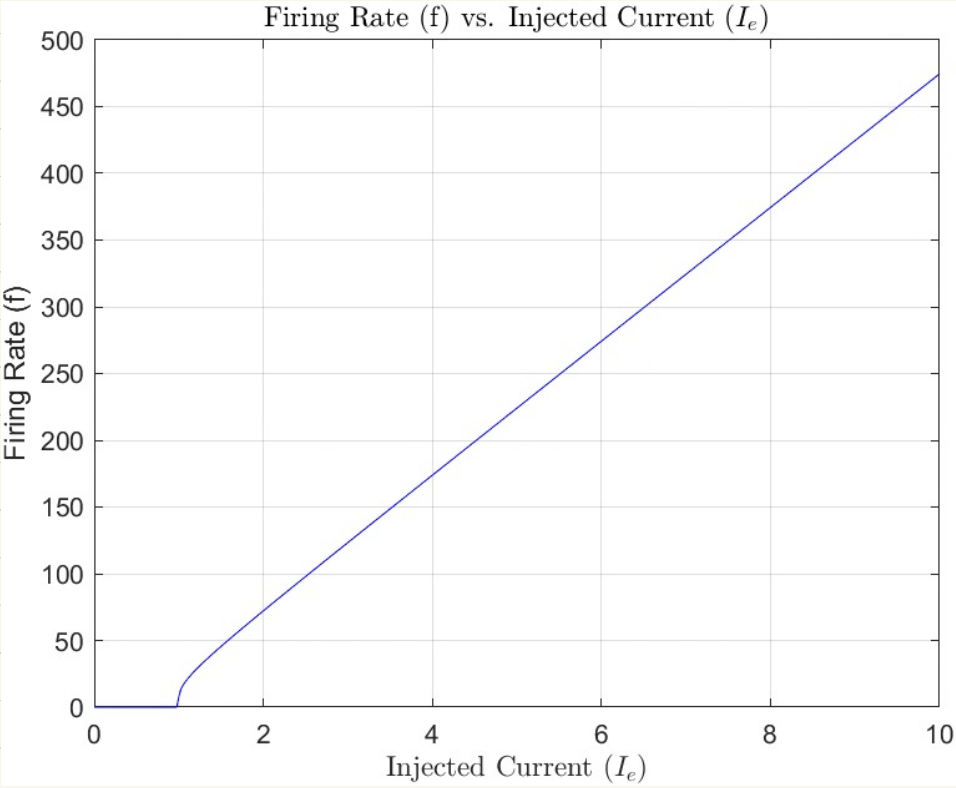
$$V = I_e + e^{\frac{C-t}{\tau}}$$

代入 $V(0)=0 \Rightarrow C = \tau \ln(-I_e) \Rightarrow V = I_e + e^{\frac{\tau\ln(-I_e) - t}{\tau}}$

代入 $V(T)=1 \Rightarrow 1 = I_e + e^{\frac{\tau\ln(-I_e) - T}{\tau}} \Rightarrow T = \tau \ln \frac{I_e}{I_e - 1}$

故 $f = \frac{1}{T} = \frac{1}{\tau} \cdot \frac{1}{\ln(1 + \frac{1}{I_e - 1})}$. 当 I_e 足够大时，由 $\ln(1+x) \to x$ 得：$f \to \frac{I_e - 1}{\tau}$. 当 I_e 足够大时，f 与 I_e 成正比.

无不应期时 f-Ie 图像：



matlab 代码：

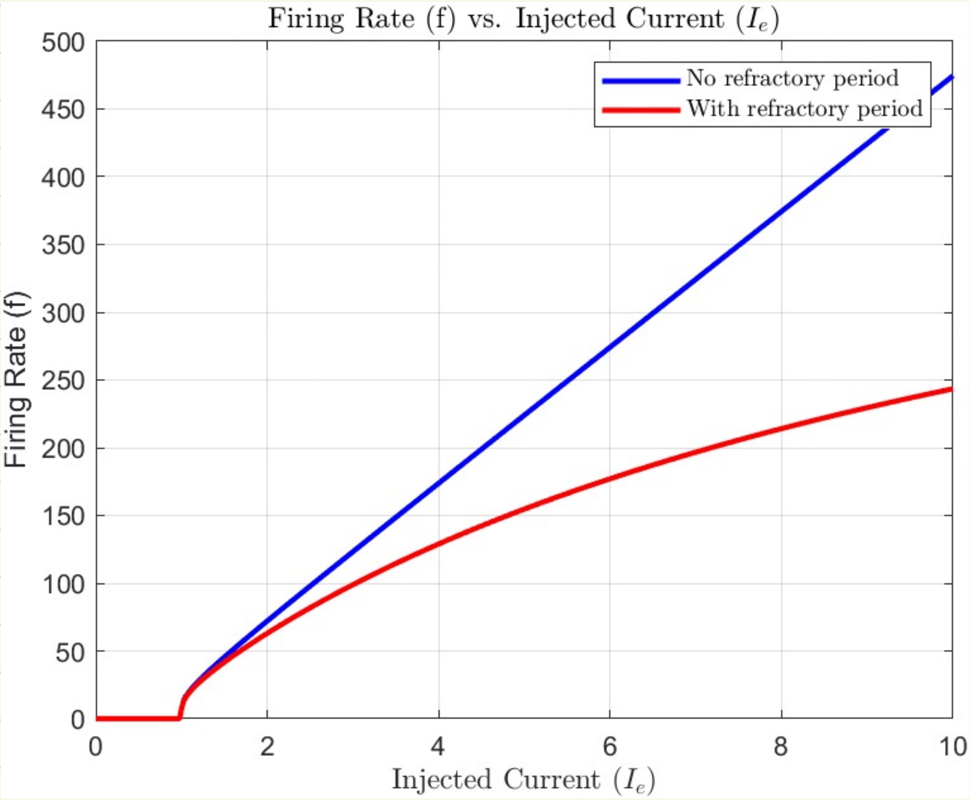
```
% Define parameters
tau = 20e-3;  % 20 ms

% Define Ie range
Ie_values = linspace(0, 10, 400);

% Calculate firing rates
f_values = zeros(size(Ie_values));
for i = 1:length(Ie_values)
    if Ie_values(i) > 1
        f_values(i) = 1 / (tau * log(Ie_values(i) / (Ie_values(i) - 1)));
    end
end

% Plot the results
figure;
plot(Ie_values, f_values, 'b');
xlabel('Injected Current ($I_e$)', 'Interpreter', 'latex');
ylabel('Firing Rate (f)');
title('Firing Rate (f) vs. Injected Current ($I_e$)', 'Interpreter', 'latex');
grid on;
```

② 有不应期时：

$$\tilde{T} = T + T_r = \tau \ln \frac{I_e}{I_e - 1} + T_r$$

$$\tilde{f} = \frac{1}{\tilde{T}} = \frac{1}{\tau \ln \frac{I_e}{I_e - 1} + T_r}$$

$f - I_e$ 图像：



matlab 代码：

```
% Define parameters
tau = 20e-3;  % 20 ms
tau_r = 2e-3;  % 2 ms

% Define Ie range
Ie_values = linspace(0, 10, 400);

% Calculate firing rates for both cases
f_no_refractory = arrayfun(@(Ie) (Ie <= 1) * 0 + (Ie > 1) * 1 / (tau * log(Ie / (Ie - 1))), Ie_values);
f_with_refractory = arrayfun(@(Ie) (Ie <= 1) * 0 + (Ie > 1) * 1 / (tau * log(Ie / (Ie - 1)) + tau_r), Ie_values);

% Plotting the results
figure;
plot(Ie_values, f_no_refractory, 'b', 'LineWidth', 2);
hold on;
plot(Ie_values, f_with_refractory, 'r', 'LineWidth', 2);
xlabel('Injected Current ($I_e$)', 'Interpreter', 'latex');
ylabel('Firing Rate (f)');
title('Firing Rate (f) vs. Injected Current ($I_e$)', 'Interpreter', 'latex');
legend('No refractory period', 'With refractory period', 'Interpreter', 'latex');
grid on;
```

Hodgkin and Huxley Model

The Hodgkin-Huxley model for generation of an action potential is constructed by a summation of leaky current, a delayed-rectified K^+ current, and a transient Na^+ current:

$$
\begin{aligned}
C_m \frac{dV}{dt} &= -\bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}}) - \bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}}) - \bar{g}_L (V - E_L) + I_e. \\
\frac{dn}{dt} &= \alpha_n (1 - n) - \beta_n n. \\
\frac{dm}{dt} &= \alpha_m (1 - m) - \beta_m m. \\
\frac{dh}{dt} &= \alpha_h (1 - h) - \beta_h h.
\end{aligned}
\tag{4}
$$

(a) Please simulate the dynamic equations and check whether it could generate action potentials. Below I will provide detailed parameter values used in Hodgkin and Huxley model.

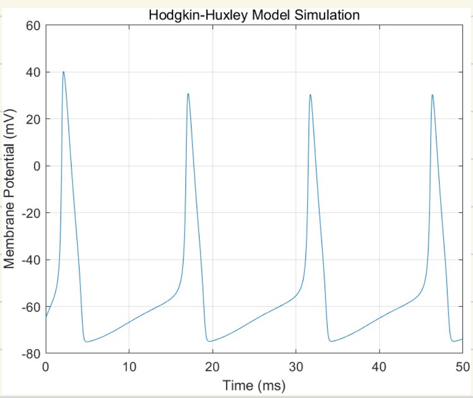
$$\alpha_n = \frac{0.01(V+55)}{1-\exp(-0.1(V+55))}, \ \beta_n = 0.125\exp(-0.0125(V+65)),$$

$$\alpha_m = \frac{0.1(V+40)}{1-\exp(-0.1(V+40))}, \ \beta_m = 4\exp(-0.0556(V+65)),$$

$$\alpha_h = 0.07\exp(-0.05(V+65)), \ \beta_h = \frac{1}{1+\exp(-0.1(V+35))}.$$

These rates have dimensions ms^{-1}. The maximal conductances and reversal potentials used in the model are $\bar{g}_{\mathrm{K}} = 0.36\ \mathrm{mS/mm}^2$, $\bar{g}_{\mathrm{Na}} = 1.2\ \mathrm{mS/mm}^2$, $\bar{g}_{\mathrm{L}} = 0.003\ \mathrm{mS/mm}^2$, $E_{\mathrm{L}} = -54.387$ mV, $E_{\mathrm{K}} = -77$ mV, $E_{\mathrm{Na}} = 50$ mV, $C_m = 10\ \mathrm{nF/mm}^2$.

由已给数据和方程，模拟得：



代码：

```
% Hodgkin-Huxley Model Parameters
Cm = 1.0;  % Membrane capacitance [uF/cm^2]
gK = 36.0;  % Maximum conductance for K+ [mS/cm^2]
gNa = 120.0;  % Maximum conductance for Na+ [mS/cm^2]
gL = 0.3;  % Maximum conductance for leak channels [mS/cm^2]
EK = -77.0;  % Reversal potential for K+ [mV]
ENa = 50.0;  % Reversal potential for Na+ [mV]
EL = -54.387;  % Reversal potential for leak channels [mV]
Ie = 10.0;  % External current [uA/cm^2]

% Rate functions
alpha_n = @(V) 0.01 * (V + 55) / (1 - exp(-0.1 * (V + 55)));
beta_n = @(V) 0.125 * exp(-0.0125 * (V + 65));
alpha_m = @(V) 0.1 * (V + 40) / (1 - exp(-0.1 * (V + 40)));
beta_m = @(V) 4 * exp(-0.0556 * (V + 65));
alpha_h = @(V) 0.07 * exp(-0.05 * (V + 65));
beta_h = @(V) 1 / (1 + exp(-0.1 * (V + 35)));

% Hodgkin-Huxley ODEs
hodgkin_huxley = @(t, y) [
    (Ie - gK * y(2)^4 * (y(1) - EK) - gNa * y(3)^3 * y(4) * (y(1) - ENa) - gL * (y(1) - EL)) / Cm;
    alpha_n(y(1)) * (1 - y(2)) - beta_n(y(1)) * y(2);
    alpha_m(y(1)) * (1 - y(3)) - beta_m(y(1)) * y(3);
    alpha_h(y(1)) * (1 - y(4)) - beta_h(y(1)) * y(4)
];

% Time vector
t_span = [0 50];

% Initial conditions
V_init = -65.0;  % Initial membrane potential [mV]
n_init = alpha_n(V_init) / (alpha_n(V_init) + beta_n(V_init));
m_init = alpha_m(V_init) / (alpha_m(V_init) + beta_m(V_init));
h_init = alpha_h(V_init) / (alpha_h(V_init) + beta_h(V_init));
initial_conditions = [V_init, n_init, m_init, h_init];

% Simulate using MATLAB's ODE solver
[t, y] = ode45(hodgkin_huxley, t_span, initial_conditions);

% Plot results
figure;
plot(t, y(:, 1));
xlabel('Time (ms)');
ylabel('Membrane Potential (mV)');
title('Hodgkin-Huxley Model Simulation');
grid on;
```

(b) Show that there is a threshold current above which the system generates periodic pulses. Explore the frequency of the pulses as a function of current, just like what you did in the integrate-and-fire model.

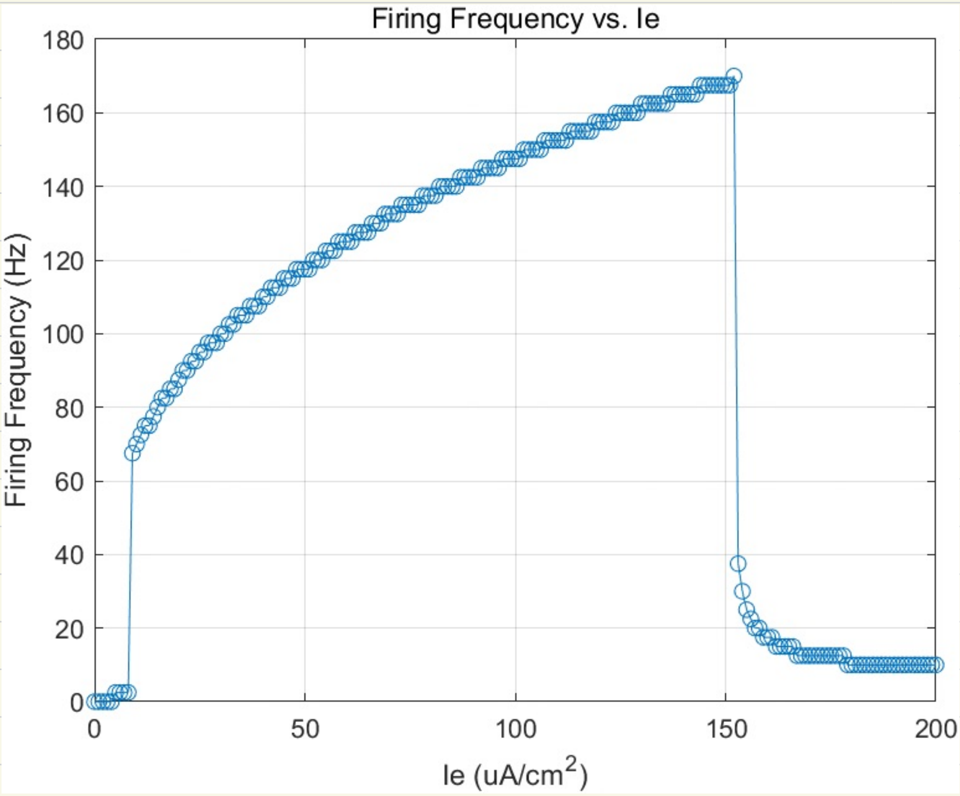
修改(a)中代码，对一系列的 Ie 值进行循环，通过检测膜电位跨越 -40mV 的次数计算放电频率.
再绘制 f-Ie 图像.

结论：

① 存在一个阈值电流($9\mu A/cm^2$)，在此电流以下，系统不产生动作电位.

② 在一定范围内，放电频率随电流的增加而增加.

③ 在某点，频率到达峰值，继续增加 Ie，f 下降。这是因为过高的输入电流导致电位始终在较高水平，没有充分的恢复时间，导致神经元进入去极化状态.

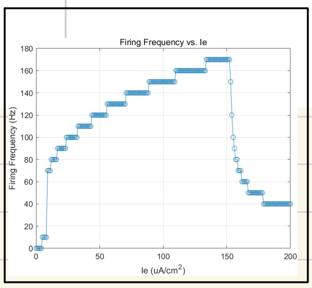


代码:

```matlab
% % Hodgkin-Huxley Model Parameters
Cm = 1.0;  % Membrane capacitance [uF/cm^2]
gK = 36.0;  % Maximum conductance for K+ [mS/cm^2]
gNa = 120.0;  % Maximum conductance for Na+ [mS/cm^2]
gL = 0.3;  % Maximum conductance for leak channels [mS/cm^2]
EK = -77.0;  % Reversal potential for K+ [mV]
ENa = 50.0;  % Reversal potential for Na+ [mV]
EL = -54.387;  % Reversal potential for leak channels [mV]

% Rate functions
alpha_n = @(V) 0.01 * (V + 55) / (1 - exp(-0.1 * (V + 55)));
beta_n = @(V) 0.125 * exp(-0.0125 * (V + 65));
alpha_m = @(V) 0.1 * (V + 40) / (1 - exp(-0.1 * (V + 40)));
beta_m = @(V) 4 * exp(-0.0556 * (V + 65));
alpha_h = @(V) 0.07 * exp(-0.05 * (V + 65));
beta_h = @(V) 1 / (1 + exp(-0.1 * (V + 35)));

% Hodgkin-Huxley ODEs
hodgkin_huxley = @(t, y, Ie) [
    (Ie - gK * y(2)^4 * (y(1) - EK) - gNa * y(3)^3 * y(4) * (y(1) - ENa) - gL * (y(1) - EL)) / Cm;
    alpha_n(y(1)) * (1 - y(2)) - beta_n(y(1)) * y(2);
    alpha_m(y(1)) * (1 - y(3)) - beta_m(y(1)) * y(3);
    alpha_h(y(1)) * (1 - y(4)) - beta_h(y(1)) * y(4)
];

% Time vector
t_span = [0 400];  % Extended time for better accuracy
```

改变此值会影响曲线的平滑程度，较小时曲线呈阶梯状

在t_span的时间跨度上计算放电次数




```matlab
% Initial conditions
V_init = -65.0;  % Initial membrane potential [mV]
n_init = alpha_n(V_init) / (alpha_n(V_init) + beta_n(V_init));
m_init = alpha_m(V_init) / (alpha_m(V_init) + beta_m(V_init));
h_init = alpha_h(V_init) / (alpha_h(V_init) + beta_h(V_init));
initial_conditions = [V_init, n_init, m_init, h_init];

% Array for various Ie values and their corresponding firing frequencies
Ie_values = 0:1:200;
frequencies = zeros(size(Ie_values));

for idx = 1:length(Ie_values)
    Ie = Ie_values(idx);
    [t, y] = ode45(@(t, y) hodgkin_huxley(t, y, Ie), t_span, initial_conditions);

    % Calculate frequency by counting the number of times V crosses -40 mV from below
    threshold_crossings = sum(diff(y(:, 1) > -40) == 1);
    frequencies(idx) = threshold_crossings / (t_span(2) - t_span(1)) * 1000;  % Convert to Hz
end

% Plot results
figure;
plot(Ie_values, frequencies, 'o-');
xlabel('Ie (uA/cm^2)');
ylabel('Firing Frequency (Hz)');
title('Firing Frequency vs. Ie');
grid on;
```