```
In [1]: import numpy as np
        import matplotlib.pyplot as plt
```

```
In [2]: def get_timeline(t_max, dt):
            return np.arange(0, t_max, dt)
```

```
In [3]: def euler(f_func, v_c, is_volt_time_dep, volt_thresh_time, n_0, t_max, dt):
            t = get_timeline(t_max, dt)
            n = np.zeros(len(t))
            n[0] = n_0

            for i in range(len(t)-1):
                if(is_volt_time_dep and (t[i] < volt_thresh_time)) :
                    v = -65
                else:
                    v = v_c
                n[i+1] = n[i] + f_func(v, n[i], t[i])*dt
            return n, t
```

1. Potassium Channel

1 (a) defining functions

```
In [4]: def alpha_n(v) :
            return 0.01*(v + 55)/(1 - np.exp(-0.1 * (v + 55)))
```

```
In [5]: def beta_n(v) :
            return 0.125 * np.exp(-0.0125 * (v + 65))
```

```
In [6]: def open_close_ion_channel_probability(v, n, t) :
            return alpha_n(v)*(1-n) - beta_n(v)*n
```

```
In [7]: def potassium_current(v, n) :
            g_k = 36 #nS
            e_k = -77 #mV
            return g_k * np.power(n,4) * (v - e_k)
```

1 (b) Activation Time Constant and Steady-State Activation

```
In [8]: def tau_n(v) :
            return 1/(alpha_n(v) + beta_n(v))
```

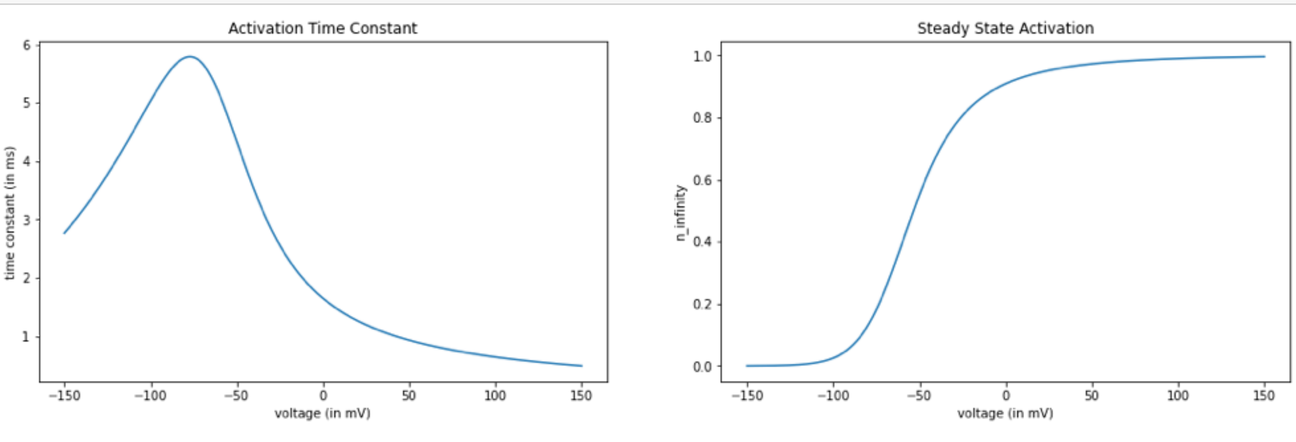
```
In [9]: def steady_state_activation_n(v) :
            return alpha_n(v)/(alpha_n(v) + beta_n(v))
```

```
In [10]: def plot_function(axes, x_range, y_range, title, x_label, y_label):
             axes.plot(x_range, y_range)
             axes.set_title(title)
             axes.set_xlabel(x_label)
             axes.set_ylabel(y_label)
```

```
In [11]: voltage_range = np.arange(-150, 150, 0.01)
```

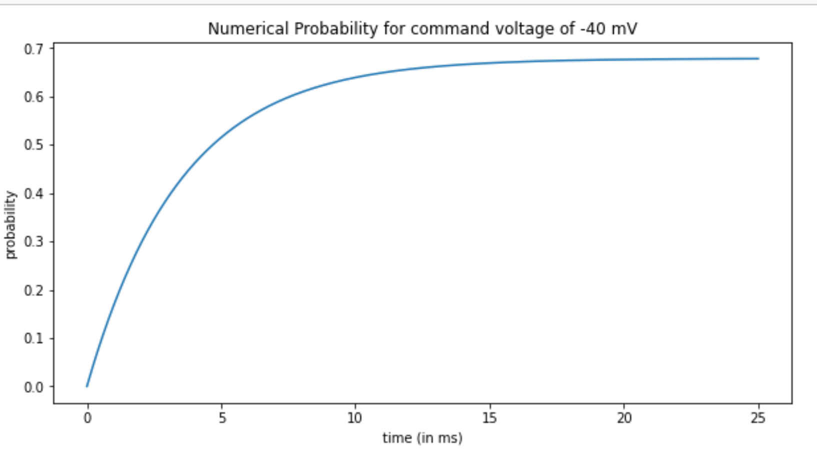
```
In [12]: tau = tau_n(voltage_range)
         n_infinity = steady_state_activation_n(voltage_range)
```

```
In [13]: fig, axes = plt.subplots(nrows=1, ncols=2, figsize=(18, 5))
         plot_function(axes[0], voltage_range, tau, 'Activation Time Constant', 'voltage (in mV)', 'time constant (in ms)')
         plot_function(axes[1], voltage_range, n_infinity, 'Steady State Activation', 'voltage (in mV)', 'n_infinity')
```




```
In [14]: n_t_0 = 0
         t_max = 25 # ms
         dt = 0.001
         v = -40 #mv
         numerical_n, t = euler(open_close_ion_channel_probability, v, False, 0,  n_t_0, t_max, dt)

         fig, axes = plt.subplots(nrows=1, ncols=1, figsize=(10, 5))
         plot_function(axes, t, numerical_n, 'Numerical Probability for command voltage of -40 mV', 'time (in ms)', 'probabilit
         y')
```




```
In [15]: numerical_n_infinity_at_23_ms = numerical_n[int(23/dt)]
         print(f'{numerical_n_infinity_at_23_ms = }')

         numerical_n_infinity_at_23_ms = 0.6776158650871139
```

The numerically calculated probability is matching with the given value in the question (approximately)

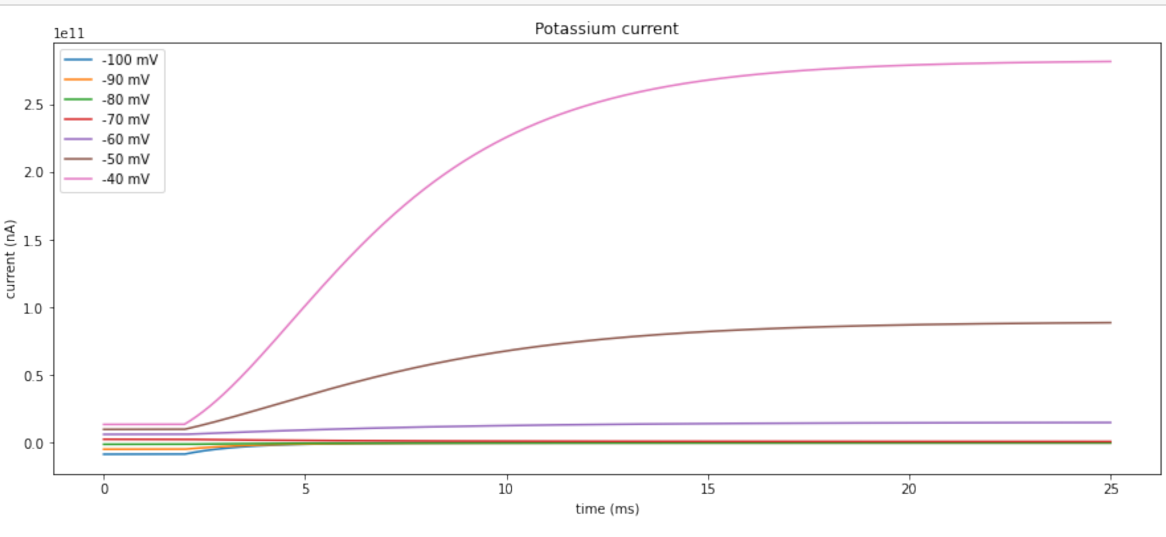
1 (c) Voltage clamp.

```
In [16]: n_t_0 = 0.3177
         t_max = 25 # ms
         dt = 0.001
         voltage_range_1c = np.arange(-100, -39, 10)#mv

         fig, axes = plt.subplots(nrows=1, ncols=1, figsize=(15, 6))

         for v_1c in voltage_range_1c :
             numerical_n, t = euler(open_close_ion_channel_probability, v_1c , True, 2,  n_t_0, t_max, dt)

             i = potassium_current(v_1c, numerical_n)
             axes.plot(t,i*1e9, label = str(v_1c) + ' mV')
             axes.set_title('Potassium current')
             axes.set_ylabel('current (nA)')
             axes.set_xlabel('time (ms)')
             axes.legend()
```



The current is zero at -70 mV and starts increases non-linearly post 2 ms if V_c increase above -70mV, however has a constant small current before 2 ms. The current flow becomes constant after almost 23 ms(can be considered as the time constant). Thus we can say that there is net flow of ions within a small time range(2ms - 23ms) with V_c above -70 mV resulting in a membrane potential.

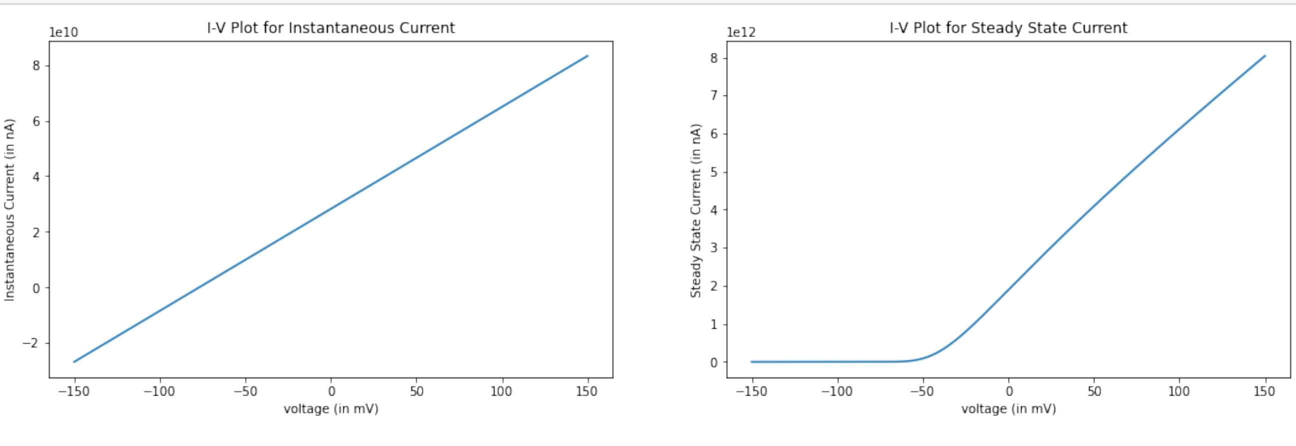
1 (d) Current-voltage relation.

```
In [17]: voltage_range = np.arange(-150, 150, 0.01)
```

```
In [18]: n_t_0 = 0.3177
         instantaneous_current = potassium_current(voltage_range, n_t_0)
```

```
In [19]: n_infinity = steady_state_activation_n(voltage_range)
         steady_state_current = potassium_current(voltage_range, n_infinity)
```

```
In [20]: fig, axes = plt.subplots(nrows=1, ncols=2, figsize=(18, 5))
         plot_function(axes[0], voltage_range, instantaneous_current*1e9, 'I-V Plot for Instantaneous Current', 'voltage (in mV
         )', 'Instantaneous Current (in nA)')
         plot_function(axes[1], voltage_range, steady_state_current*1e9, 'I-V Plot for Steady State Current', 'voltage (in mV)'
         , 'Steady State Current (in nA)')
```



2. Sodium ion channel

2 (a) Write all necessary functions and plot the steady-state activation and time constant of m and h as a function of the membrane potential.

```
In [21]: def sodium_current(v, m, h) :
             g_na = 120 #nS
             e_na = 50 #mV
             return g_na * np.power(m,3) * h * (v - e_na)
```

```
In [22]: def alpha_m(v) :
             return 0.1*(v + 40)/(1 - np.exp(-0.1 * (v + 40)))
```

```
In [23]: def beta_m(v) :
             return 4 * np.exp(-0.0556 * (v + 65))
```

```
In [24]: def alpha_h(v) :
             return 0.07 * np.exp(-0.05 * (v + 65))
```

```
In [25]: def beta_h(v) :
             return 1/(1 + np.exp(-0.1 * (v + 35)))
```

```
In [26]: def open_close_ion_channel_probability_m(v, m, t) :
             return alpha_m(v)*(1-m) - beta_m(v)*m
```

```
In [27]: def open_close_ion_channel_probability_h(v, h, t) :
             return alpha_h(v)*(1-h) - beta_h(v)*h
```

```
In [28]: def tau_m(v) :
             return 1/(alpha_m(v) + beta_m(v))

         def tau_h(v) :
             return 1/(alpha_h(v) + beta_h(v))
```

```
In [29]: def steady_state_activation_m(v) :
             return alpha_m(v)/(alpha_m(v) + beta_m(v))

         def steady_state_activation_h(v) :
             return alpha_h(v)/(alpha_h(v) + beta_h(v))
```

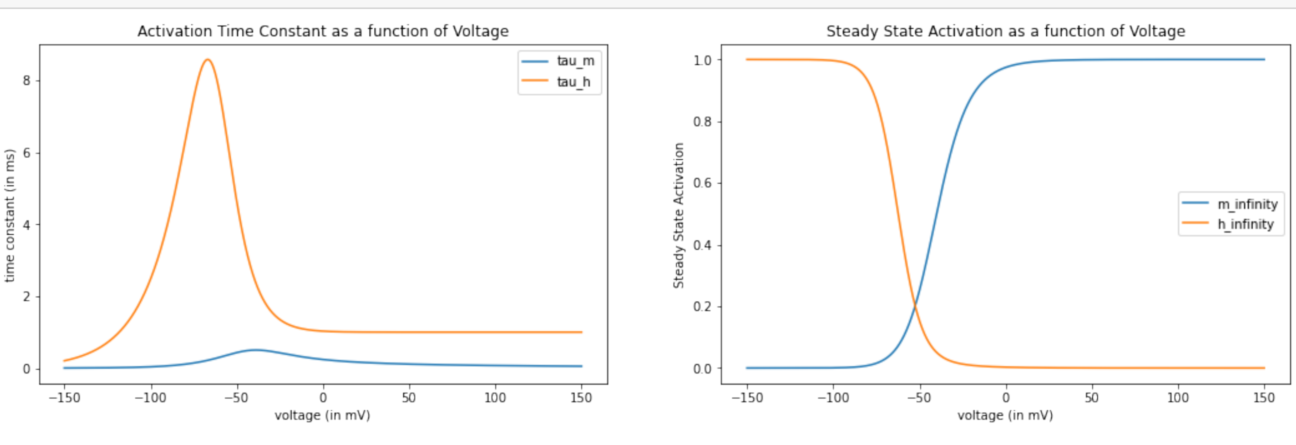
```
In [30]: def plot_function_with_label(axes, x_range, y_range, title, x_label, y_label, label_m):
             axes.plot(x_range, y_range, label = label_m)
             axes.set_title(title)
             axes.set_xlabel(x_label)
             axes.set_ylabel(y_label)
             axes.legend()
```

```
In [31]: tau_m = tau_m(voltage_range)
         m_infinity = steady_state_activation_m(voltage_range)

         tau_h = tau_h(voltage_range)
         h_infinity = steady_state_activation_h(voltage_range)
```

```
In [32]: fig, axes = plt.subplots(nrows=1, ncols=2, figsize=(18, 5))
         plot_function_with_label(axes[0], voltage_range, tau_m, 'Activation Time Constant as a function of Voltage', 'voltage
         (in mV)', 'time constant (in ms)', 'tau_m')
         plot_function_with_label(axes[0], voltage_range, tau_h, 'Activation Time Constant as a function of Voltage', 'voltage
         (in mV)', 'time constant (in ms)', 'tau_h')

         plot_function_with_label(axes[1], voltage_range, m_infinity, 'Steady State Activation as a function of Voltage', 'volt
         age (in mV)', 'Steady State Activation', 'm_infinity')
         plot_function_with_label(axes[1], voltage_range, h_infinity, 'Steady State Activation as a function of Voltage', 'volt
         age (in mV)', 'Steady State Activation', 'h_infinity')
```



Activation time constant tau_m becomes much flatter when compared to tau_n, where as tau_h(a little high) is much comparable with tau_n

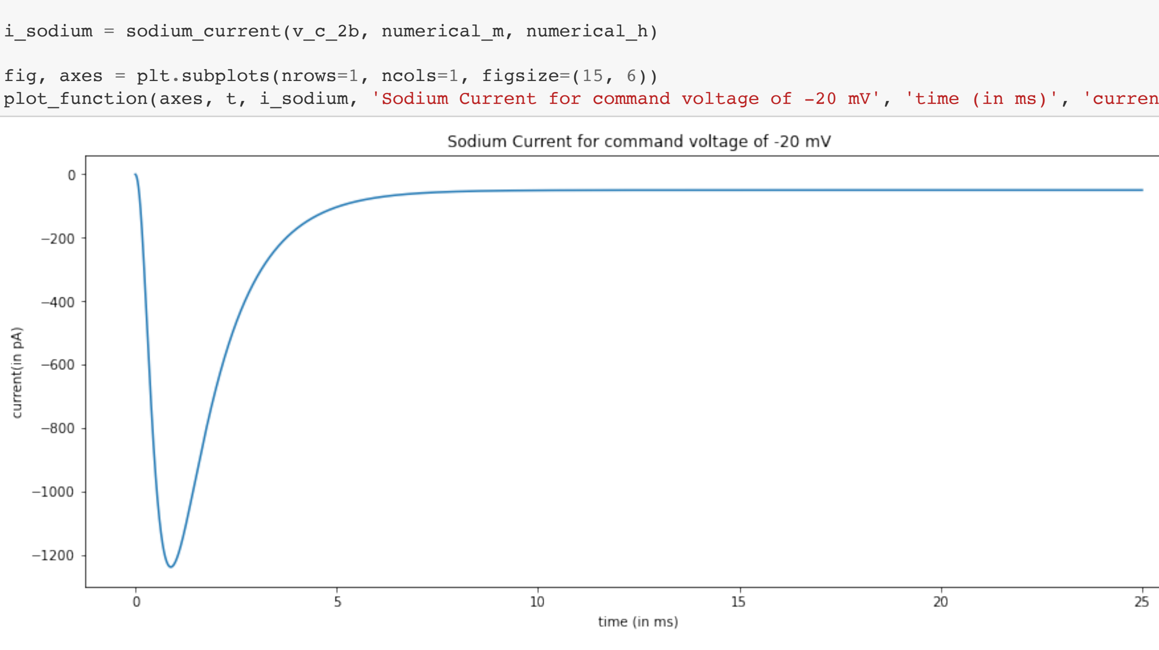
m_infinity is increasing with increase in voltage similar to n_infinity whereas h_infinity is decreasing with the increase in voltage

2 (b) Simulate and plot the sodium current

```
In [52]: m_t_0 = 0.0529
         h_t_0 = 0.5961
         t_max = 25 # ms
         dt = 0.001
         v_c_2b = -20 #mv
         numerical_m, t = euler(open_close_ion_channel_probability_m, v_c_2b, False, 0,  m_t_0, t_max, dt)
         numerical_h, t = euler(open_close_ion_channel_probability_h, v_c_2b, False, 0,  h_t_0, t_max, dt)

         i_sodium = sodium_current(v_c_2b, numerical_m, numerical_h)

         fig, axes = plt.subplots(nrows=1, ncols=1, figsize=(15, 6))
         plot_function(axes, t, i_sodium, 'Sodium Current for command voltage of -20 mV', 'time (in ms)', 'current(in pA)')
```




```
In [41]: min_current = min(i_sodium)
         print(f'{min_current=}')

         -1239.2303835547104
```

This is matching with the minimum current given in the exercise (approximately)

```
In [44]: steady_state_current_at_15 = i_sodium[int(15/dt)]
         print(steady_state_current_at_15)

         -50.499348537265206
```

The steady current at 15 ms is also matching with the steady state current given in the exercise (approximately)

2 (c) Simulate the voltage clamp experiment for the sodium current

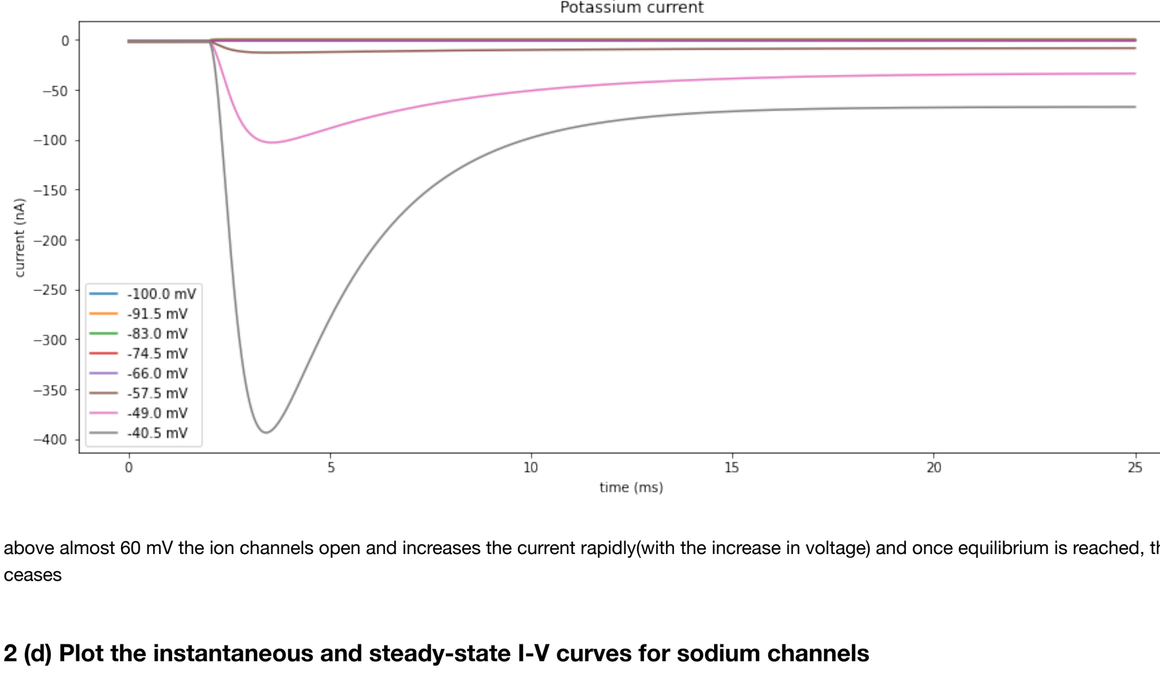
```
In [68]: m_t_0 = 0.0529
         h_t_0 = 0.5961
         t_max = 25 # ms
         dt = 0.001
         voltage_range_2c = np.arange(-100, -39, 8.5)#mv

         fig, axes = plt.subplots(nrows=1, ncols=1, figsize=(15, 6))

         for v_c_2c in voltage_range_2c :
             numerical_m, t = euler(open_close_ion_channel_probability_m, v_c_2c , True, 2,  m_t_0, t_max, dt)
             numerical_h, t = euler(open_close_ion_channel_probability_h, v_c_2c , True, 2,  h_t_0, t_max, dt)

             i_sodium_2c = sodium_current(v_c_2c, numerical_m, numerical_h)
             axes.plot(t, i_sodium_2c, label = str(v_c_2c) + ' mV')

         axes.set_title('Potassium current')
         axes.set_ylabel('current (nA)')
         axes.set_xlabel('time (ms)')
         axes.legend();
```



above almost 60 mV the ion channels open and increases the current rapidly(with the increase in voltage) and once equilibrium is reached, the current flow ceases

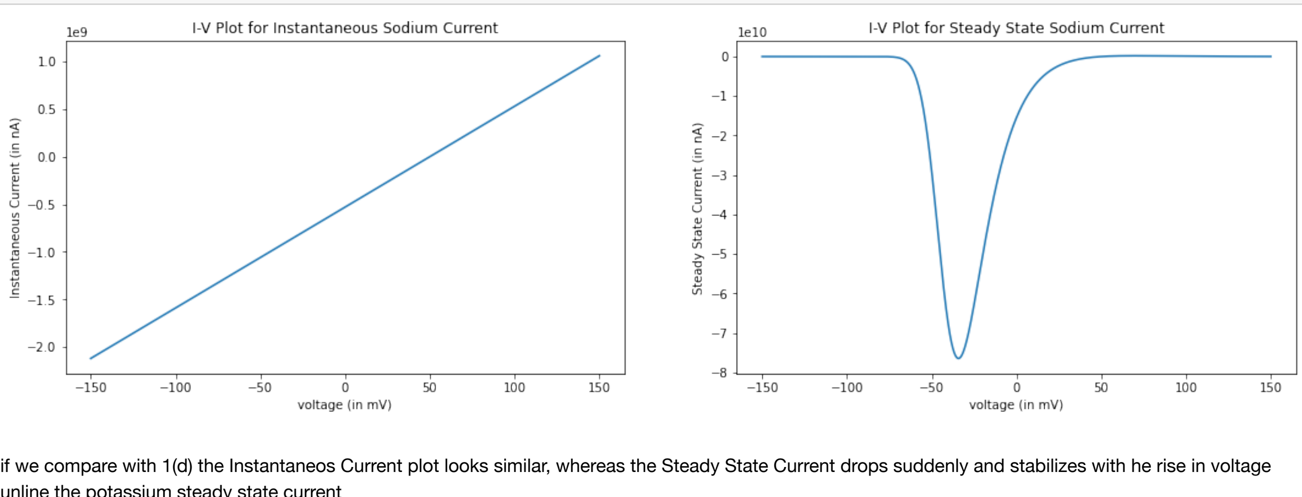
2 (d) Plot the instantaneous and steady-state I-V curves for sodium channels

```
In [69]: voltage_range_2d = np.arange(-150, 150, 0.01)
```

```
In [70]: m_t_0 = 0.0529
         h_t_0 = 0.5961
         instantaneous_sod_current = sodium_current(voltage_range_2d, m_t_0, h_t_0)
```

```
In [71]: m_infinity = steady_state_activation_m(voltage_range_2d)
         h_infinity = steady_state_activation_h(voltage_range_2d)
         steady_state_sod_current = sodium_current(voltage_range_2d, m_infinity, h_infinity)
```

```
In [72]: fig, axes = plt.subplots(nrows=1, ncols=2, figsize=(18, 5))
         plot_function(axes[0], voltage_range_2d, instantaneous_sod_current*1e9, 'I-V Plot for Instantaneous Sodium Current', '
         voltage (in mV)', 'Instantaneous Current (in nA)')
         plot_function(axes[1], voltage_range_2d, steady_state_sod_current*1e9, 'I-V Plot for Steady State Sodium Current', 'vo
         ltage (in mV)', 'Steady State Current (in nA)')
```



if we compare with 1(d) the Instantaneos Current plot looks similar, whereas the Steady State Current drops suddenly and stabilizes with he rise in voltage unline the potassium steady state current

```
In [ ]:
```