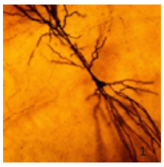
Models of a single neuron

Lectures 4-5



Outline

- Electrical properties of neurons
- Integrate and fire model

- Model of synaptic input
- What this model can and cannot explain
- Other models

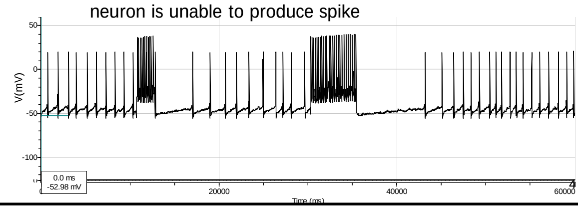
- Based on Dayan & Abbott
  - Sections 5.1-5.4, 5.8-5.9

Membrane potential

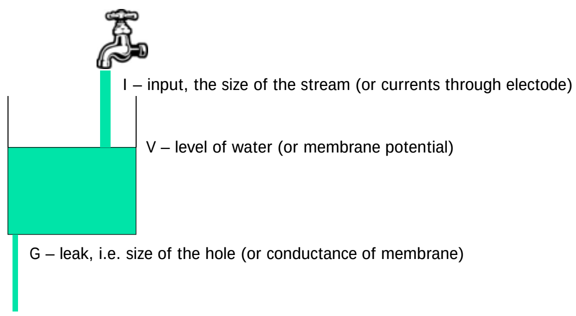
- Potential inside the neuron lower than outside
  - Positively charged ions have higher concentration outside than inside the neuron
    - Ion pumps remove certain positively charged ions from inside (full story later)
  - Membrane potential, V = the difference between the potential inside and outside the neuron
  - Resting membrane potential $E_L \approx$ -70 mV
  - Inputs from other neurons change the potential
    - Inputs from excitatory neurons increase V
    - Inputs from inhibitory neurons decrease V
    - Details later

Spikes

- When V exceeds threshold $V_{th} \approx$ -40mV, V rapidly increases for a brief period (~1ms)
- After a spike
  - The potential decays to $V_{reset} \approx$ -65 mV
  - There is a brief refractory period of ~2 ms in which the neuron is unable to produce spike



Neurons and water buckets



Description of a system

- System that changes in time is described by
  - Initial condition
    - E.g. V(0)=0
  - Equation describing its changes in small time interval dt
    - E.g. dV=(I - GV)dt
    - The leak is proportional to
      - Size of the hole
      - Level of water
    - Note that dV is proportional to dt

Euler method

- From the initial condition and the equation we can find the states of the system in all future time points
  - V(t+dt) = V(t) + dV
  - V(t+dt) = V(t) + dt (I – G V(t))
- Example V(0)=0, I=1, G=1, dt=0.01
  - V(0.01) = V(0) + 0.01 (1 – 1 V(0)) = 0.01
  - V(0.02) = 0.01 + 0.01 (1 – 1 0.01) = 0.0199
  - V(0.03) = ...

Simple case

- It is very easy to find future states of the system in Matlab, if we make two assumptions:
  - dt = 1
    - Then the equation simplifies to:
    - V(t+1) = V(t) + I – G V(t)
  - Initial time = 1, e.g. V(1)=0
- E.g. assume we want to solve for t = 1:50, and we choose I = 0.1, G=0.1

Matlab implementation

- I = 0.1;
- G = 0.1;
- MAXT = 50;
- V(1) = 0;
- for t = 1:MAXT-1
-     V(t+1) = V(t) + I – G*V(t);
- end
- plot (V);

Mapping of indices

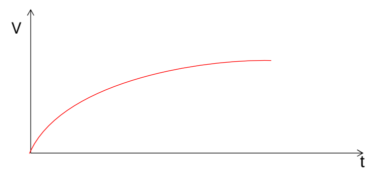
- But in most cases we want dt < 1
- Assume we want to solve the equation on interval [0,5] with dt=0.01
  - We want to compute:
  - V(t) for t=[0:0.01:5];
  - But in Matlab we need to store them in a vector indexed by positive integers:
  - V(i) for i=[1:1:501];
- Thus we need to remember that i does not correspond to t when we plot it

Matlab implementation

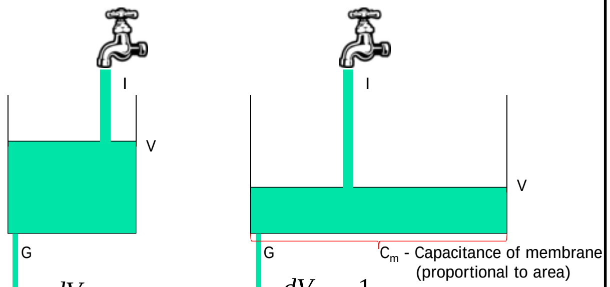
- I = 1;
- G = 1;
- dt = 0.01;
- MAXT = 5;
- V(1) = 0;
- for i = 1:MAXT/dt
-     V(i+1) = V(i) + dt*(I – G*V(i));
- end
- plot ([0:dt:MAXT], V);

Rate of change

- The equation dV=(I-GV)dt is usually written: dV/dt = I – GV
- dV/dt is the derivative and describes the slope of water level as a function of time:



Size of the bucket matters



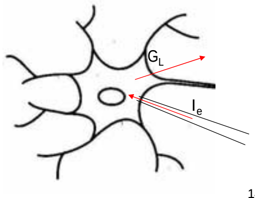
$$\frac{dV}{dt} = I - GV$$

$$\frac{dV}{dt} = \frac{1}{C_m}(I - GV)$$

Back to neurons...

- We will now gradually add elements to the “bucket equation” so it describes neurons
- Let us make notation more specific
  - “Leak conductance” G_L
  - Current injected by electrode I_e
- Hence:

$$C_m \frac{dV}{dt} = I_e - G_L V$$



Leakage current

- Leakage current includes
  - Currents due to channels with constant conductance
  - Currents due to pumps
  - They drive V to a particular value
  - Thus leak becomes

$$C_m \frac{dV}{dt} = I_e - G_L (V - E_L)$$

  - E_L – resting potential, or Equilibrium for Leak
  - Note: leak if $V > E_L$, but no leak when $V = E_L$

Integrate and fire model

- Integrate: $C_m \frac{dV}{dt} = -G_L (V - E_L) + I_e$
  - or $\tau_m \frac{dV}{dt} = E_L - V + R_m I_e$
  - Where:
    - Time constant $\tau_m = C_m / G_L$
    - Membrane resistance $R_m = 1/G_L$
- And fire:
  - IF $V > V_{th}$, THEN Generate a spike; $V = V_{reset}$

Simulations

- Euler method can be used for simulations
- For the purpose of Euler method the equation can be formulated as:

$$\frac{dV}{dt} = \frac{1}{\tau_m}(E_L - V + R_m I_e)$$

- In every step of integration
  - IF $V > V_{th}$, THEN set $V = V_{reset}$

Will the neuron fire?

- We can ask:
  - If we inject current I, will the neuron fire?
- Methods of answering this question
  - Brute force method
    - Solve the differential equation and check if it intersects threshold
  - Clever method
    - Calculate the voltage, to which neuron would converge in absence of threshold, i.e. the attractor
      - It can be done without solution of the differential equation - details on the next slide...
    - If this voltage is above threshold, the neuron will fire

Finding attractors

- In the attractor, system does not change, hence the derivative is equal to 0
  - Example: E_L=-70, V_{th}=-40, I = 3, R_m=5
    - We substitute:

$$0 = -70 - V + 5*3$$

    - And solve V* = -55
- Points in which the derivative is equal to 0 are called fixed points
- Not all fixed points are attractors (there is easy way to check it), but this one is.

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Minimum current required for firing

- In summary:
  - The fixed point V* satisfies:

$$0 = E_L - V^* + R_m I_e$$

  - hence

$$V^* = E_L + R_m I_e$$

- The neuron will fire if $V^* > V_{th}$, i.e.

$$E_L + R_m I_e > V_{th}$$

  - hence

$$I_e > \frac{V_{th} - E_L}{R_m}$$

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Chemistry 101

- All you need to know about chemistry:
  - Ions are particles with electric charge
    - That can be either positive or negative
  - Different ions have different names, and are denoted by e.g. Na^+ ← Sign

    Chemical symbol
  - Ions of opposite sign attract each other
  - Ions of the same sign are pushed away

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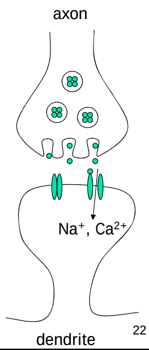
Excitatory synaptic transmission

- After an excitatory neuron produces an action potential, synapses at the ends of its axon release excitatory neurotransmitter
- This neurotransmitter binds to certain receptors, which opens ion channels permeable to positively charged ions (Na^+, Ca^{2+})
- Flow of positively charged ions increases membrane potential



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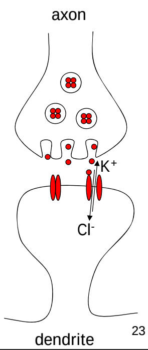
Inhibitory synaptic transmission

- After an inhibitory neuron produces an action potential, synapses at the ends of its axon release inhibitory neurotransmitter
- This neurotransmitter binds to certain receptors, which opens ion channels permeable to:
  - K^+ which have higher concentration inside the neuron
  - Negatively charged Cl^-
- Flow of these ions decreases membrane potential



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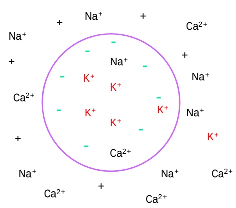
Concentration of ions

- Pumps move
  - Na^+ and Ca^{2+} outside
  - K^+ inside
- This results in
  - Negative V
  - Imbalance of concentration



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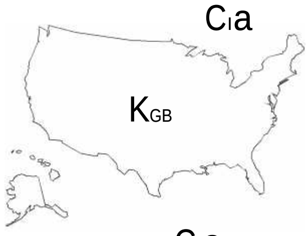
The way to remember this...

Na_{SA} Na_{SA}

$C_l a$

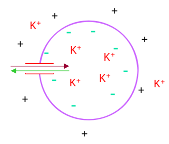
$C_l a$ K_{GB} $C_l a$



$C_l a$

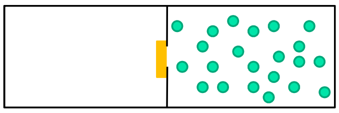
Flow of ions

- Membrane includes channels permeable to specific ions
- Let us first consider K^+
- Flow depends on:
  - Electrical gradient
  - Chemical gradient



Chemical gradient

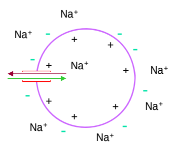
- Analogy with gas:
  - What would happen if the barrier were opened?



- Similarly, the ions of a particular type have a tendency move to areas where their concentration is lower

Equilibrium potential

- Equilibrium potential = Membrane potential at which electrical and chemical gradient balance each other, for a give type of ions
- Equilibrium potential for different ions
  - E_K: -70 to -90mV
  - E_{Na}: >50mV, E_{Ca}: ~150mV
    - These ions have higher concentration outside
    - So at the equilibrium:
      - Electrical gradient
      - Chemical gradient

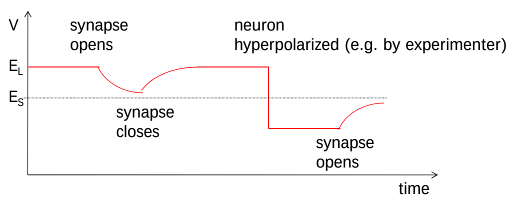


Ion flow through a synapse

- Synapse permeable to a combination of ions
- Equilibrium potential of a synapse
  - Depends on the equilibrium potentials of the ions it is permeable to
  - Denoted by E_S
- When synapse open, V changes towards E_S
- Excitatory synapses have $E_S > 0$
  - So if open, always increase V

Inhibitory synapse

- Inhibitory synapses typically have $E_S < E_L$
  - Normally flow decreases V
  - But if neuron hyperpolarized $V < E_S$
    - The flow of ion reverses and increases V



Current through a synapse

- As with leak, we define the synaptic current: $I = -G_S\,(V-E_S)$
- Check
  - If $V=E_S$ then no current flow
  - If $V>E_S$ then $V-E_S > 0$; $I < 0$; $V\downarrow$
  - If $V<E_S$ then $V-E_S < 0$; $I > 0$; $V\uparrow$
- G_S - conductance of synapse when open
  - Depends on the number and type of channels
  - Often called synaptic weight

Synaptic input

- Input at time t:

$$C_m \frac{dV}{dt} = -G_L(V-E_L) - P_S G_S (V-E_S) + I_e$$

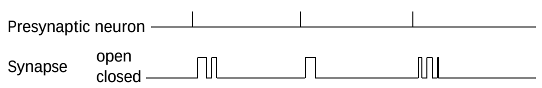
  - Where P_s - probability of synapse being open
- After dividing by G_L:

$$\tau_m \frac{dV}{dt} = E_L - V - R_m P_S G_S (V-E_S) + R_m I_e$$

  - Recall $R_m=1/G_L$

Synaptic dynamics

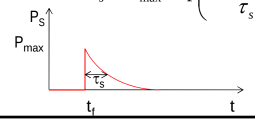
- After pre-synaptic (input) neuron fires
  - While neurotransmitter is bound to synaptic channels, they rapidly switch between open and closed state
  - Neurotransmitter is bound for a variable period
  - For example:



Opening probability

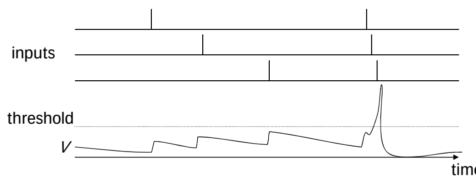
- Let us assume a very simple model:
  - The neurotransmitter binds immediately after firing of the pre-synaptic (input) neuron
    - The opening probability reaches maximum: $P_s=P_{max}$
    - t_f – time of the recent firing of pre-synaptic neuron
  - Then it decays with time constant τ_s

$$P_s = P_{\max} \exp\left(-\frac{t-t_f}{\tau_s}\right)$$



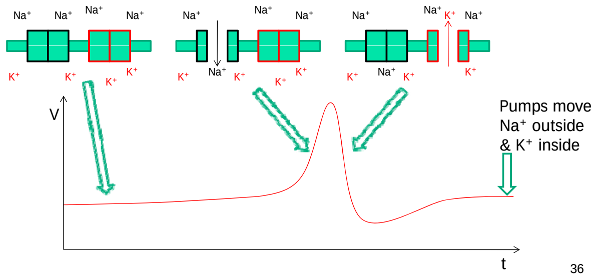
The model can explain

- Firing rate of a neuron depends on the firing rate of its inputs
- Firing rate of a neuron depends on how synchronized its inputs are



The model cannot explain (1)

- Spike generation



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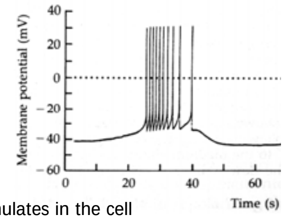
Hodgkin & Huxley model

$$\begin{aligned}
C\frac{dv}{dt} &= I - \underbrace{g_{Na}m^3h(V-V_{Na})}_{Na^+} - \underbrace{g_K n^4(V-V_K)}_{K^+} - g_L(V-V_L)\\
\frac{dm}{dt} &= a_m(V)(1-m) - b_m(V)m\\
\frac{dh}{dt} &= a_h(V)(1-h) - b_h(V)h\\
\frac{dn}{dt} &= a_n(V)(1-n) - b_n(V)n\\
a_m(V) &= .1(V+40)/(1-\exp(-(V+40)/10))\\
b_m(V) &= 4\exp(-(V+65)/18)\\
a_h(V) &= .07\exp(-(V+65)/20)\\
b_h(V) &= 1/(1+\exp(-(V+35)/10))\\
a_n(V) &= .01(V+55)/(1-\exp(-(V+55)/10))\\
b_n(V) &= .125\exp(-(V+65)/80)
\end{aligned}$$

Nobel prize, 1963

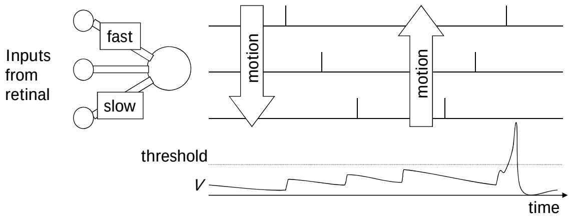
The model cannot explain (2)

- The dependence of spike production on concentration of ions inside a neuron
  - E.g. bursting neurons
    - Mechanism:
    - During firing Ca^{2+} cumulates in the cell
    - High concentration of Ca^{2+} opens "Ca^{2+} dependent K^+ channels" which block firing until Ca^{2+} is pumped out
  - Additional equation describing Ca^{2+} concentration can be added to Hodgkin & Huxley equations



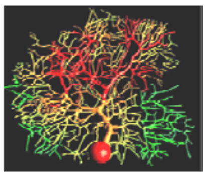
The model cannot explain (3)

- Temporal propagation of potential inside of the neuron
  - E.g. critical for neurons detecting direction of motion



Compartmental models

- The model neuron consists of a number of compartments
  - Each described by Hodgkin & Huxley equations extended with terms describing flow from adjacent compartments
- Explain propagation of potential inside a neuron



Simpler models of neuron

- Continuous models
  - Firing rate of neuron *i* described by a continuous variable x_i
  - E.g. linear model: $\dfrac{dx_i}{dt} = -kx_i + \sum_{inputs\ j} w_{ij}x_j$
- Binary model (McCulloch & Pitts, 1943)
  - The neuron is in one of two states
    - Active: $x_i = 1$, or inactive $x_i = 0$
  - $x_i = \begin{cases} 1 & if \ \sum_{inputs\ j} w_{ij}x_j > T \\ 0 & otherwise \end{cases}$

Summary

- Neurons integrate signals from their inputs
- When their membrane potential exceeds a threshold, they produce action potentials
- Integrate and fire model
  - Explains dependence of neuronal firing rate on firing rate and synchrony of its inputs
- Choosing appropriate level (Dayan & Abbott):
  "Oversimplified models can, of course, give misleading results, but extensively detailed models can obscure interesting results beneath inessential an unconstrained complexity."