Synaptic Model (2):

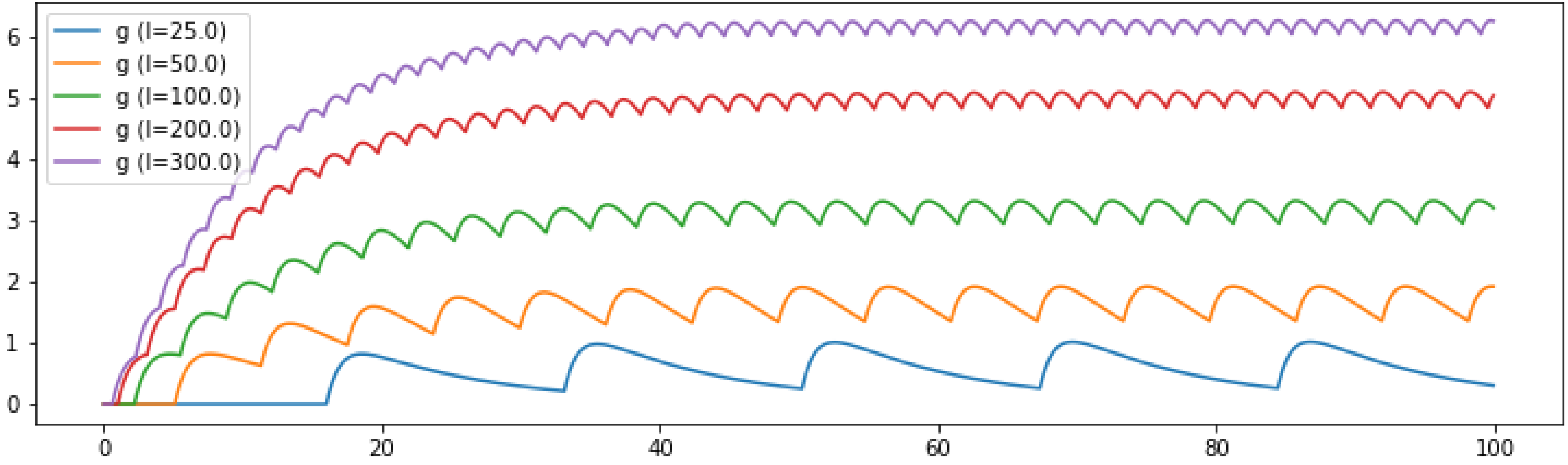
Kinetic/Markov Models

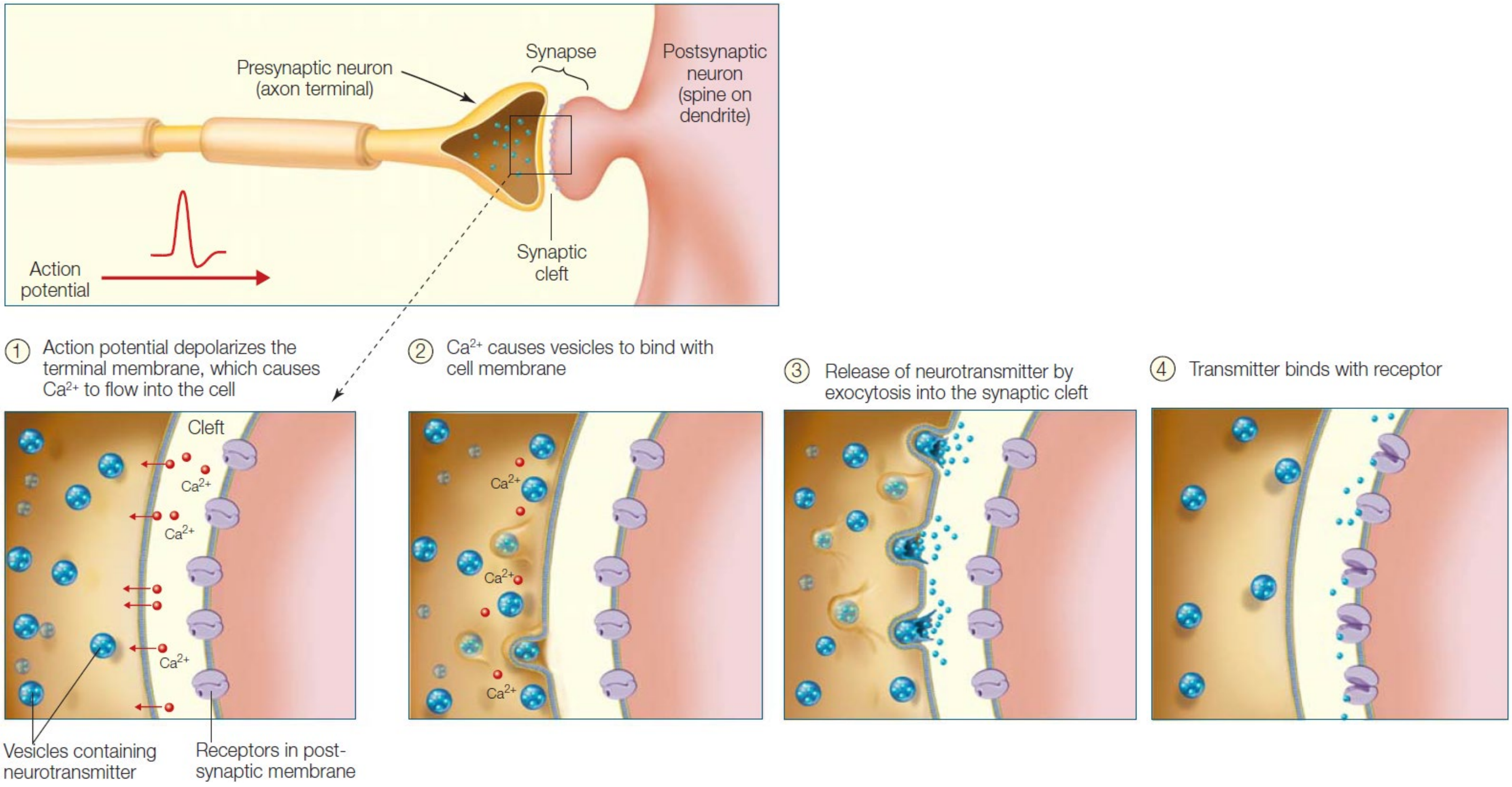
Neuron models	HH neuron model
	LIF neuron model
	Exponential IF model
Synapse models	Exponential/Alpha synapse
	AMPA/GABA/NMDA synapse
Network Models	E/I balance network
	Continuous attractor network
	Working memory model
	Decision making model

Kinetic Models

The problem of the phenomenological models

- A significant limitation of the simple waveform description of synaptic conductance is that it does not capture <u>the actual behavior seen at many synapses when trains of action potentials arrive</u>.
- A new release of neurotransmitter soon after a previous release should not be expected to contribute as much to the postsynaptic conductance due to saturation of postsynaptic receptors by previously released transmitter and the fact that some receptors will already be open.





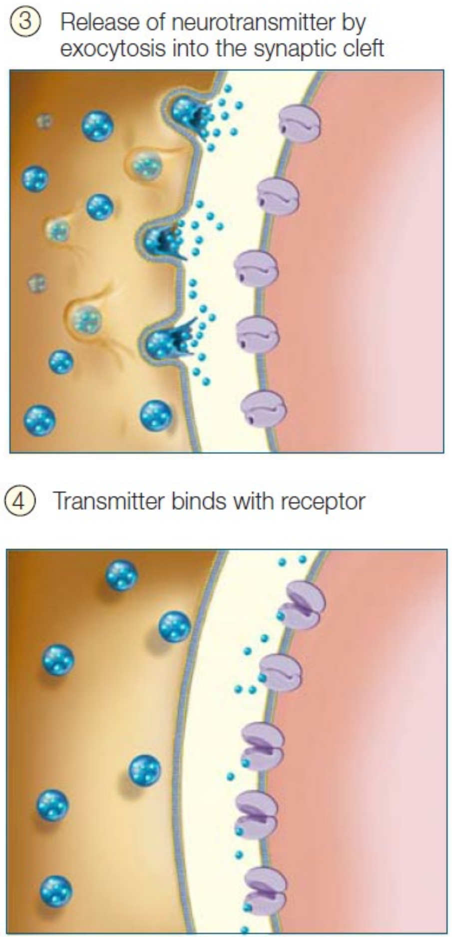
Presynaptic neuron (axon terminal)
Synapse
Postsynaptic neuron (spine on dendrite)
Action potential
Synaptic cleft
1 Action potential depolarizes the terminal membrane, which causes Ca^{2+} to flow into the cell
2 Ca^{2+} causes vesicles to bind with cell membrane
3 Release of neurotransmitter by exocytosis into the synaptic cleft
4 Transmitter binds with receptor
Cleft
Ca^{2+}
Vesicles containing neurotransmitter
Receptors in post-synaptic membrane

Kinetic/Markov models

The simplest kinetic model is a two-state scheme in which receptors can be either closed, C, or open, O, and the transition between states depends on transmitter concentration, $[T]$, in the synaptic cleft:

$$\mathrm{C} \underset{\beta}{\overset{\alpha[\mathrm{T}]}{\rightleftharpoons}} \mathrm{O},$$

- α and β are voltage-independent forward and backward rate constants.

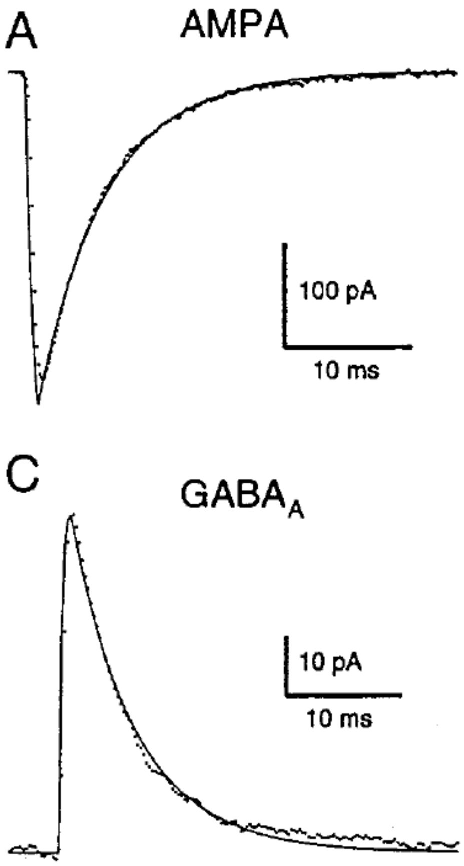


C and O can range from 0 to 1, and describe the fraction of receptors in the closed and open states, respectively.

The synaptic conductance is:

$$g_{\mathrm{syn}}(t) = \overline{g}_{\mathrm{syn}} \mathrm{O}(t).$$

AMPA/GABAA synapse model



$$\underset{\text{(close)}}{1-s} \underset{\beta}{\overset{\alpha[T]}{\rightleftharpoons}} \underset{\text{(open)}}{s}$$

$$\frac{ds}{dt} = \alpha[T](1-s) - \beta s$$

$$I = \bar{g}s(V-E)$$

- $\alpha[T]$ denotes the transition probability from state (1−s) to state (s)
- β represents the transition probability of the other direction
- E is a reverse potential, which can determine whether the direction of I is inhibition or excitation.

- $E = 0\ mV$ => Excitatory synapse [AMPA]
- $E = -80\ mV$ => Inhibitory synapse [GABAA]

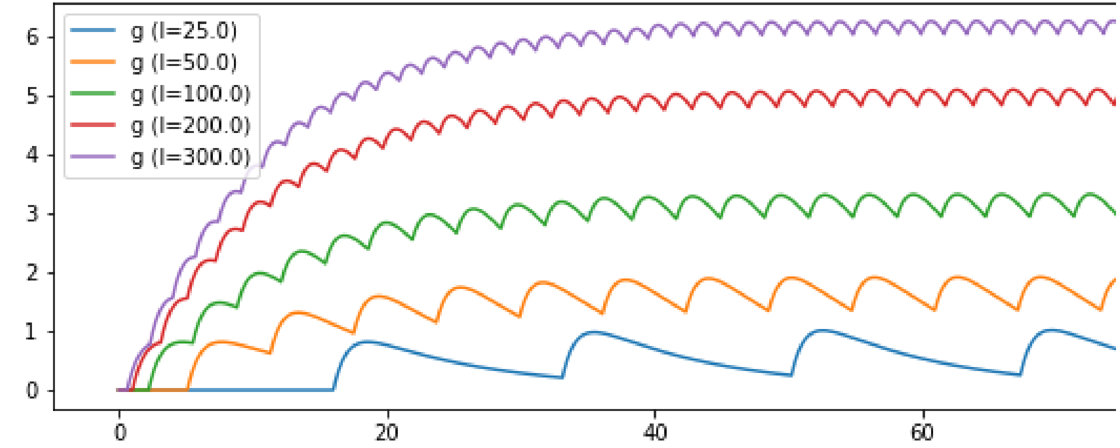
Comparison

Dual Exponential Model

$$g_{\text{syn}}(t) = \bar{g}_{\text{syn}} g$$

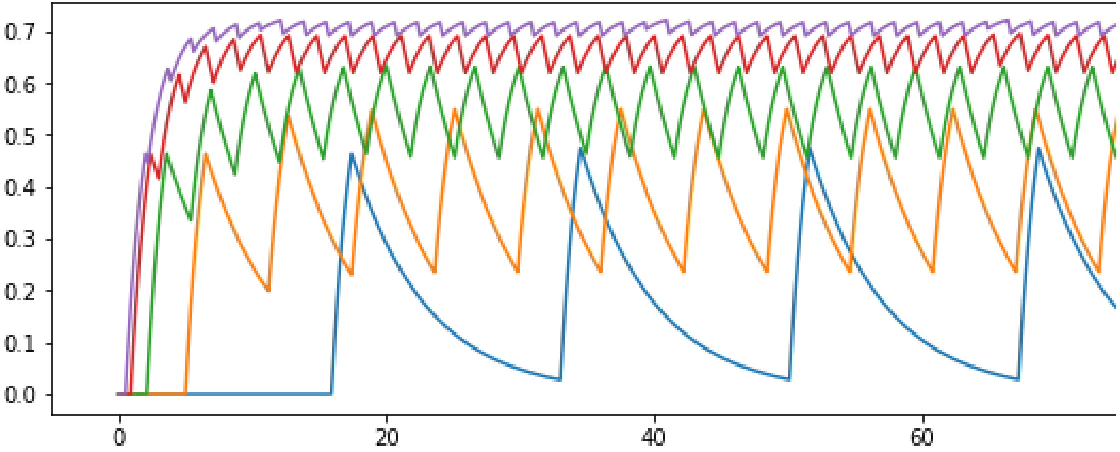
$$\frac{dg}{dt} = -\frac{g}{\tau_{\text{decay}}} + h$$

$$\frac{dh}{dt} = -\frac{h}{\tau_{\text{rise}}} + \delta(t_0 - t),$$

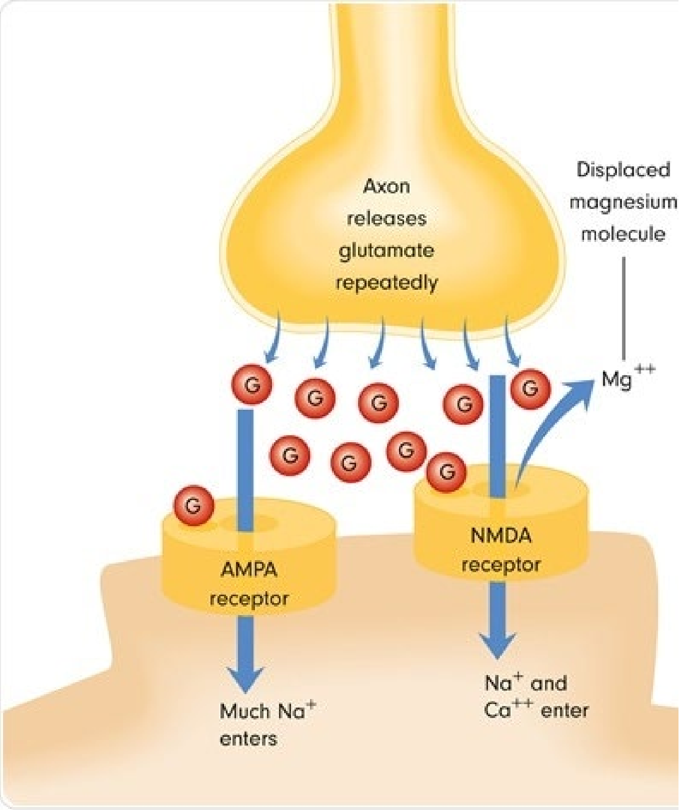


AMPA kinetic Model

$$\frac{ds}{dt} = \alpha[T](1 - s) - \beta s$$



NMDA synapse model



$$\frac{ds}{dt} = \alpha[T](1-s) - \beta s$$

$$I = \bar{g} s B(V)(V - E)$$

$$B(V) = \frac{1}{1 + \exp(-0.062V)[Mg^{2+}]_o/3.57}$$

- The magnesium block of the NMDA receptor channel is an extremely fast process compared to the other kinetics of the receptor (Jahr and Stevens 1990a, 1990b). The block can therefore be accurately modeled as an instantaneous function of voltage(Jahr and Stevens 1990b).

- where $[Mg^{2+}]_o$ is the external magnesium concentration (1 to 2mM in physiological conditions)

Conclusion: Markov model for gating channel modeling

Voltage-dependent gating (Hodgkin-Huxley)	$C \underset{\beta(V)}{\overset{\alpha(V)}{\rightleftarrows}} O$	$\frac{d[O]}{dt} = \alpha(1-[O]) - \beta[O]$
Transmitter gating	$C + n\mathrm{Ca_i} \underset{\beta}{\overset{\alpha}{\rightleftarrows}} O$	$\frac{d[O]}{dt} = \alpha[T]^n(1-[O]) - \beta[O]$
Calcium-dependent gating	$C + n\mathrm{Ca_i} \underset{\beta}{\overset{\alpha}{\rightleftarrows}} O$	$\frac{d[O]}{dt} = \alpha[Ca_i]^n(1-[O]) - \beta[O]$
Two-stage gating	$R_0 + T \underset{K2}{\overset{K1}{\rightleftarrows}} R \underset{K3}{\overset{K4}{\rightleftarrows}} D$	$\frac{d[R]}{dt} = K_1[T](1-[R]-[D]) - K2[R] + K_3[D]$ $\frac{d[D]}{dt} = K_4[R] - K_3[D]$

AMPA/GABAA synapse coding

```python
class AMPA(bp.TwoEndConn):
    target_backend = ['numpy', 'numba']

    def __init__(self, pre, post, conn, alpha=0.98, beta=0.18, g_max=0.5,
                 E=0., T=0.5, T_duration=0.5, delay=1., **kwargs):
        # parameters
        self.alpha, self.beta = alpha, beta
        self.T, self.T_duration = T, T_duration
        self.E, self.g_max = E, g_max
        self.delay = delay

        # connections
        self.conn = conn(pre.size, post.size)
        self.pre_ids, self.post_ids = conn.requires('pre_ids', 'post_ids')
        self.size = len(self.pre_ids)

        # variables
        self.s = bp.ops.zeros(self.size)
        self.t_last_pre_spike = -1e7 * bp.ops.ones(self.size)
        self.g = self.register_constant_delay('g', size=self.size, delay_time=delay)

        super(AMPA, self).__init__(pre=pre, post=post, **kwargs)
```

```python
@staticmethod
@bp.odeint(method='exponential_euler')
def derivative(s, t, TT, alpha, beta):
    ds = alpha * TT * (1 - s) - beta * s
    return ds

def update(self, _t):
    for i in range(self.size):
        pre_id, post_id = self.pre_ids[i], self.post_ids[i]

        # update
        if self.pre.spike[pre_id]: self.t_last_pre_spike[pre_id] = _t
        TT = ((_t - self.t_last_pre_spike[pre_id]) < self.T_duration) * self.T
        self.s[i] = self.int_s(self.s[i], _t, TT, self.alpha, self.beta)
        self.g.push(i, self.g_max * self.s[i])

        # output
        self.post.input[post_id] -= self.g.pull(i) * (self.post.V[post_id] - self.E)
```

Exercise

1. Implement AMPA synapse model

2. Implement $GABA_A$ synapse model