Theoretical & computational Neuroscience:
Programming the Brain

(BM 6140)

2-credit

Modeling of synapses

1. Realistic modeling by converting biological phenomena into mathematical models

2. Simplify to guess an expression for g as function of pre synaptic voltage

   Treat it as a parallel conductance model

3. Direct injection of current waveform

Markov models and system dynamics

$$X \underset{\beta}{\overset{\alpha}{\rightleftarrows}} y$$

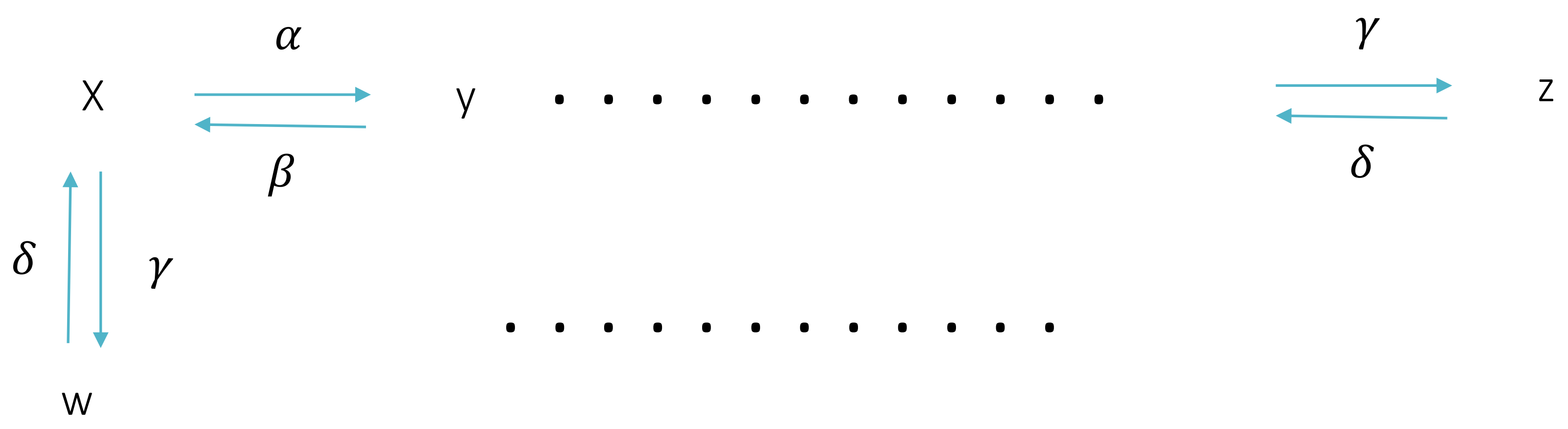
What are the corresponding differential equations ?

$$\frac{dx}{dt} = -\alpha x + \beta y$$

$$\frac{dy}{dt} = \alpha x - \beta y$$

Segev, Koch, Methods in neuronal modeling

Markov models and system dynamics



$$\frac{dx}{dt} = -\Sigma \alpha_{xi} i + \Sigma \beta_{jx} j$$

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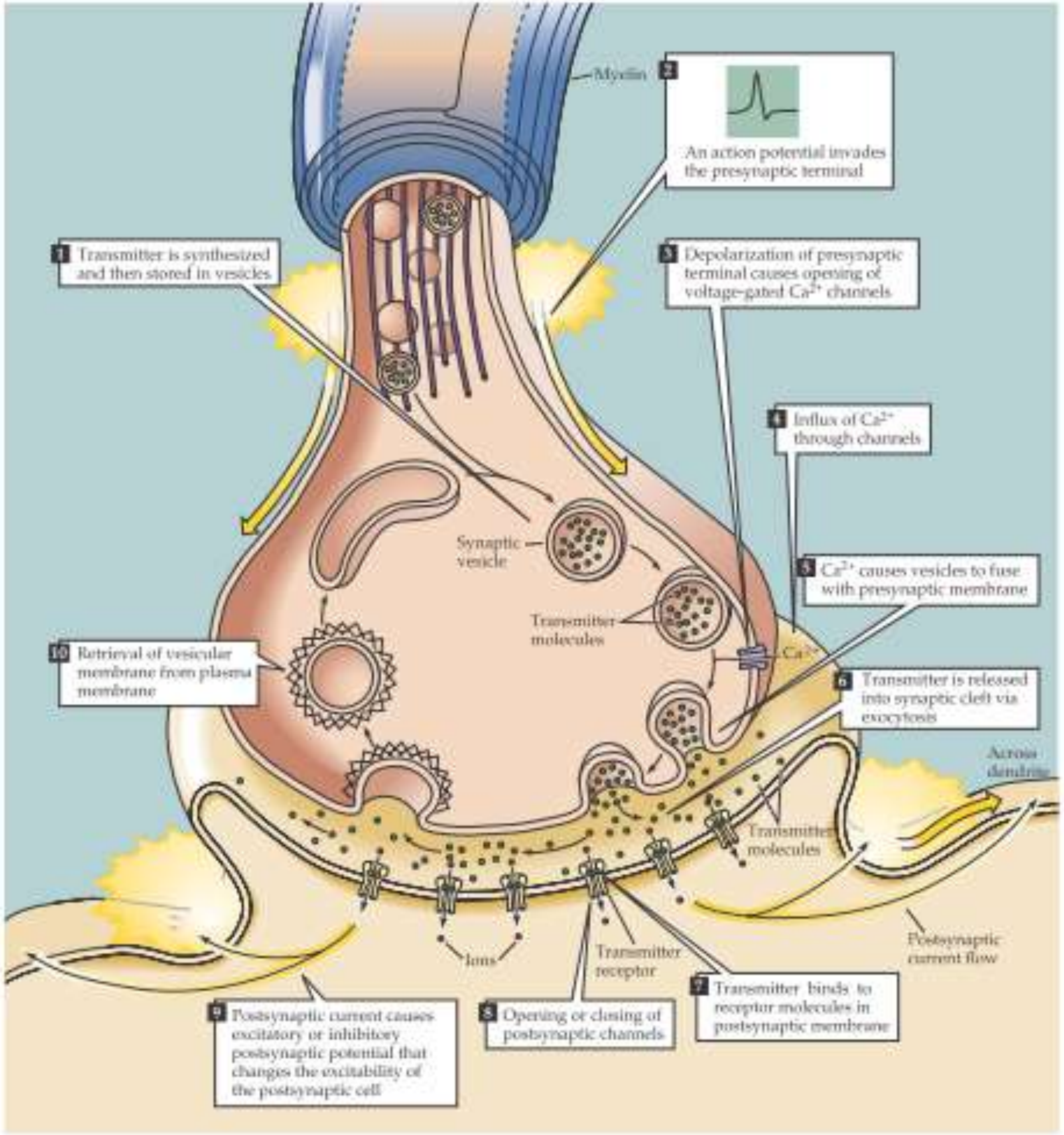
Chemical synapse (revisited)

Event sequence



Pre synaptic dynamics

E.g. AMPA

$$4\,\mathrm{Ca}^{2+} + X \underset{k_u}{\overset{k_b}{\rightleftharpoons}} X^*$$

$$X^* + V_e \underset{k_2}{\overset{k_1}{\rightleftharpoons}} V_e^* \xrightarrow{k_1} nT\,.$$

Segev, Koch, Methods in neuronal modeling

Post synaptic dynamics (AMPA)

$$\begin{array}{ccccccc} C_0 & \underset{R_{u_1}}{\overset{R_b T}{\rightleftharpoons}} & C_1 & \underset{R_{u_2}}{\overset{R_b T}{\rightleftharpoons}} & C_2 & \underset{R_c}{\overset{R_o}{\rightleftharpoons}} & O \\ & & R_d \downarrow\uparrow R_r & & R_d \downarrow\uparrow R_r & & \\ & & D_1 & & D_2, & & \end{array}$$

where the unbound form of the receptor C_0 binds to one molecule of transmitter T, leading to the singly bound form C_1, which itself can bind another molecule of T leading to the doubly bound form C_2. R_b is the binding rate, and R_{u1} and R_{u2} are unbinding rates. Each form C_1 and C_2 can desensitize, leading to forms D_1 and D_2, with rates R_d and R_r for desensitization and resensitization, respectively. Finally, the doubly bound receptor C_2 can open, leading to the open form O,

$$I_{AMPA} = \bar{g}_{AMPA}[O](V - E_{AMPA}),$$

Segev, Koch, Methods in neuronal modeling

Results : kinetic model of pre-syn release

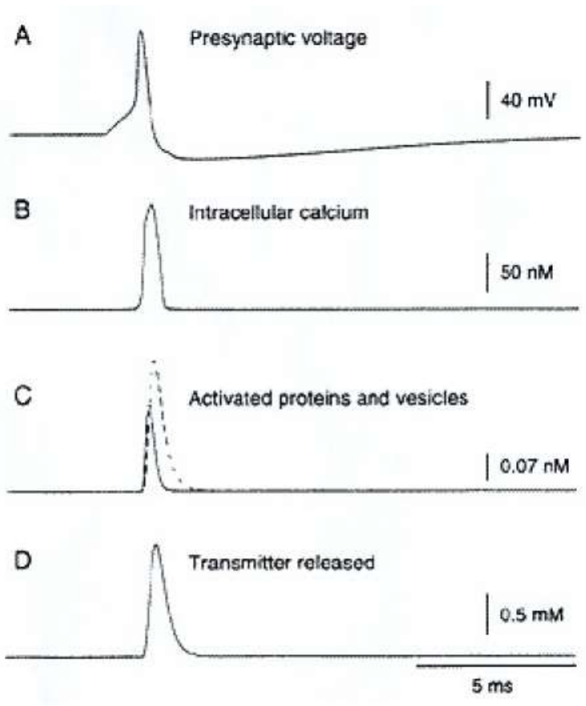


Figure 1.1

Kinetic model of presynaptic release.
(A) A presynaptic action potential was elicited by injection of a 0.1 nA current pulse lasting 2 msec in the presynaptic terminal.
(B) Intracellular Ca^{2+} concentration in the presynaptic terminal. A high-threshold calcium current was also present and provided a transient calcium influx during the action potential. Removal was provided by an active calcium pump.
(C) Relative concentration of activated calcium-binding protein X* (solid line) and vesicles V_e^* (dotted line).
(D) Concentration of transmitter in the synaptic cleft.

Simplifications by curve fit

$$[T](V_{pre}) = \frac{T_{max}}{1 + \exp[-(V_{pre} - V_p)/K_p)},$$

$$C + T \underset{\beta}{\overset{\alpha}{\rightleftharpoons}} O,$$

$$I_{AMPA} = \bar{g}_{AMPA} r (V - E_{AMPA}),$$

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

R is the number of channels in open state

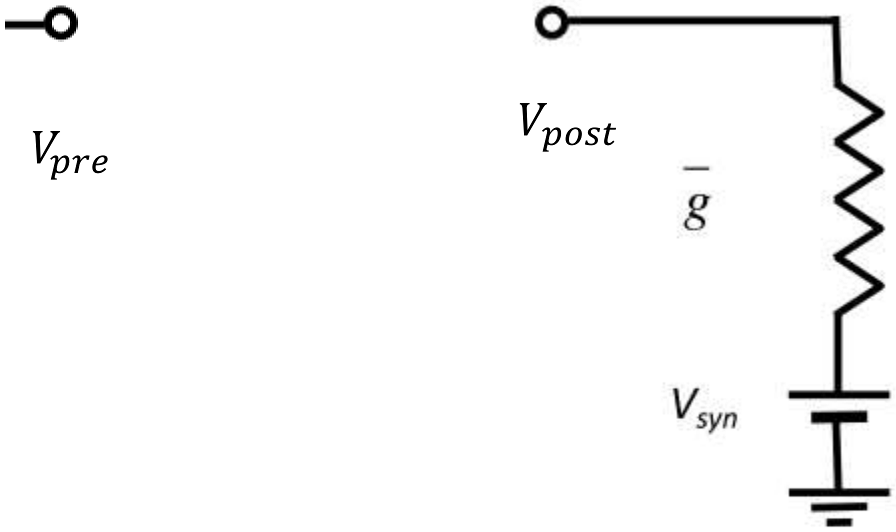
[T] directly calculated using curve fits..

Helps in autonomous evaluation of multiple neurons

Method 2 : Parallel conductance

$$I_{AMPA} = \overline{g}g(V_{pre}(t))(V_{post} - E_{AMPA})$$

g is a conductance waveform calculated using the waveform of pre synaptic voltage.



Method 3 : Direct current injections

Direct injection of current waveform in post synaptic neuron triggered by firing of pre synaptic neuron

$$\frac{C_m dV}{dt} = -g\,(V - E_L) + I_{syn}(t)$$

Using kinetic schemes in NEURON

```
STATE { mc m }
KINETIC scheme1 {
    ~ mc <-> m (a(v), b(v))
}
```

Reactants $\quad mc \underset{b(v)}{\overset{a(v)}{\rightleftarrows}} m \quad$ Products

is equivalent to

```
STATE { mc m }
DERIVATIVE scheme1 {
    mc' = -a(v)*mc + b(v)*m
    m'  =  a(v)*mc - b(v)*m
}
```

The tilde "~" is used to distinguish this kind of statement from other sequences of tokens

Slide Courtesy : Rishikesh Narayanan, MBU, IISC