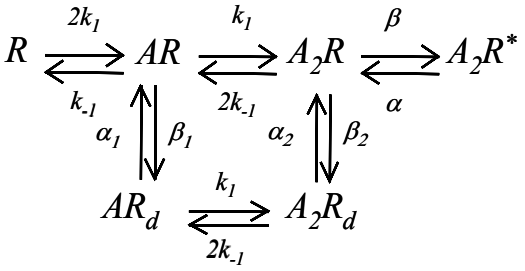
9.16 – Electrophysiology

Homework set #3

Examination of the kinetic properties of AMPA and NMDA receptors

The kinetic steps of glutamate receptor activation following the release of transmitters can be summarized in the general scheme illustrated in the right panel.



The following set of equations can be used to simulate the process of glutamate receptor activation.

$$\frac{dAR}{dt} = 2k_1[A]R + 2k_{-1}A_2R + \alpha_1 AR_d - (k_1[A] + k_{-1} + \beta_1)AR$$

$$\frac{dA_2R}{dt} = k_1[A]AR + \alpha A_2R^* + \alpha_2 A_2R_d - (\beta + 2k_{-1} + \beta_2)A_2R$$

$$\frac{dA_2R^*}{dt} = \beta A_2R - \alpha A_2R^*$$

$$\frac{dAR_d}{dt} = \beta_1 AR + 2k_{-1}A_2R_d - (k_1[A] + \alpha_1)AR_d$$

$$\frac{dA_2R_d}{dt} = \beta_2 A_2R + k_1[A]AR_d - (2k_{-1} + \alpha_2)A_2R_d$$

where

$$R = 1 - AR - A_2R - A_2R^* - AR_d - A_2R_d$$

R is the glutamate receptor, A the concentration of the neurotransmitter, AR the receptor with a single transmitter molecule binding, A2R the receptor with two transmitter molecules binding, and A2R* the receptor in an open channel configuration. Therefore, the probability of channel opening after neurotransmitter release Po is determined by A2R*.

The kinetic rate constants for AMPA receptors are

$k_1 = 0.01$ $k_{-1} = 4.8$

$\alpha = 0.5$ $\beta = 9$

$\alpha_1 = 0.005$ $\beta_1 = 1.2$

$\alpha_2 = 0.8$ $\beta_2 = 0.6$

The kinetic rate constants for NMDA receptors are

$k_1 = 0.002 \quad k_{-1} = 0.008$

$\alpha = 0.16 \quad \beta = 0.009$

$\alpha_1 = 0.005 \quad \beta_1 = 0.0035$

$\alpha_2 = 0.005 \quad \beta_2 = 0.0035$

The concentration of glutamate in the synaptic cleft can be imitated by

$$A(t) = A_{MAX}\left(3.2\exp^{-t/0.1} + 0.5\exp^{-t/2.1}\right) * \left(1 - \exp^{-t/0.2}\right)$$

where A_{max} is the peak concentration of transmitters. During the process of synaptic transmission, A_{max} can vary from 100 μM up to 3000 μM.

A. Solve the above equations numerically using MATLAB and answer the following questions.

1. What determines the decay phase of an EPSC, the profile of glutamate concentration or intrinsic properties of the channel? Does the decay phase of AMPA or NMDA receptor activation depend upon the glutamate concentration?
2. Describe the behavior of AMPA vs NMDA receptors under repetitive activation. Can one increase AMPA receptor activation by repetitive release of transmitter? What about NMDA receptors?