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Queueing Model for Presynaptic Events of Neuron

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Abstract: The communication in the biological systems are evolved and perfected over a period of time in the process of natural evolution. The biological systems adopt integrative approach to maintain homeostasis and are really complex to resolve. The modeling approach not only helps one to understand but also to quantify the biological processes. The events in presynaptic neuron which are critical for communication are surprisingly synonymous with the well established queueing model theory. An attempt has been made to understand the events in presynaptic neuron in terms of queueing model.

Keywords: Queueing model, Presynaptic events, Neurotransmission

INTRODUCTION

The most of the communication in biological systems involve electrical and chemical synapses. Chemical synapses are more abundant than electrical synapse in a nervous system. Messages move from one location to another in the form of action potentials (AN) along axons. These electrical events are also known as nerve impulses. At a synapse involving two neurons, the impulse passes through pre synaptic neuron (SN) to the post SN.A synapse may be electrical, for example, vestibular nuclei in which direct physical contact between cells exists by gap junctions. In a chemical synapse, neurotransmitter (NT) is used to spread signals. The main difference between electrical synapse (ES) and chemical synapse (CS) is spread of impulse in multidirectional and unidirectional respectively. The situation at CS is far more dynamic than that an ES, because the cells are not directly coupled. The arriving AN at a CS may or may not release enough chemical to bring the post SN to threshold. In addition, other factors may also intervene and make the post SN more or less sensitive to the arriving stimuli. In summary, post SN is not solely dependent on pre SN as it can be adjusted by variety of factors.

More than 50 chemical substances have been proved or postulated to act as NT. They are grossly classified as: rapidly acting small molecules and slowly acting neuropeptides. In most cases, the small molecules are synthesized in the cytosol of the pre SN and or packed into phospho lipid vesicles by means of special transporters by active transport mechanisms. Then each time an AP reaches synaptic terminal. A few vesicles at a time release their content NT into synaptic cleft. This usually happens within a millisecond or less by fusion of vesicular membranes with pre SN followed by exocitosis. During exocitosis, the NT is poured into the synaptic cleft. The vesicles that store and release small molecule NT is continuously recycled and used over and over again. The fusion of vesicles with synaptic membrane are mediated by special proteins called as SNAPs and VAMPs which are present on pre synaptic membrane and vesicular membrane respectively. During fusion the vesicular membrane becomes a part of synaptic membrane. However, within seconds the vesicle portion of membrane retracts inside to form an empty vesicle. The details of the synaptic events are diagrammatically depicted in Figure 1.

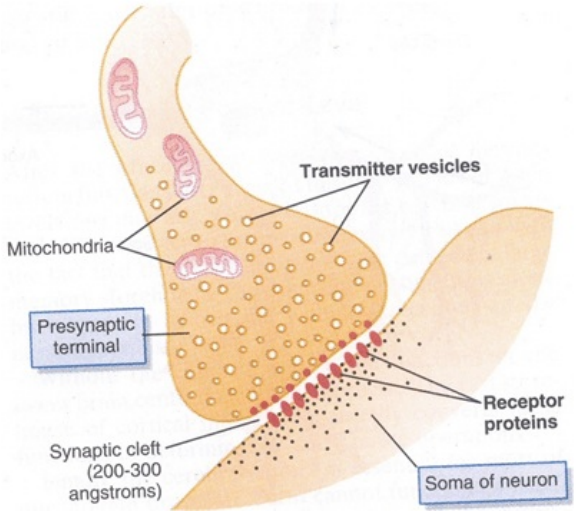

Fig. 1: Physiologic anatomy of the synapse[1]

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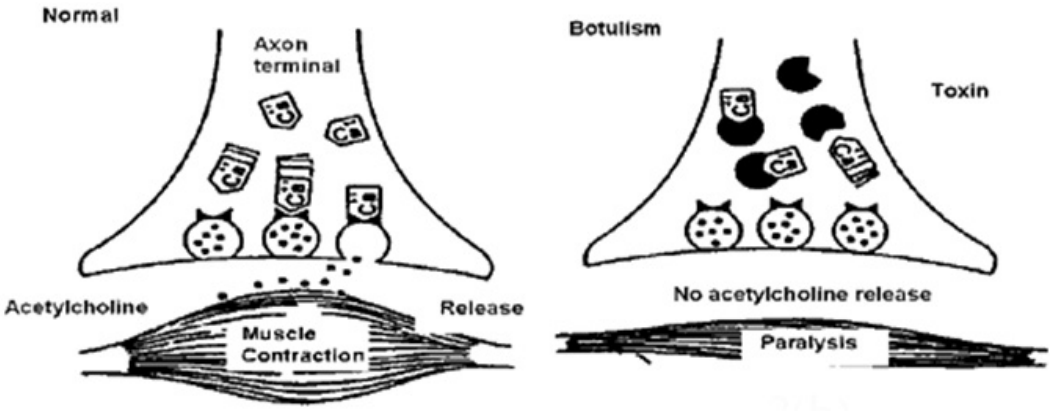

(2a) **(2b)**

Fig. 2: Cholinergic synapse at neuro muscular junction

The ACh (acetylcholine) is a typical small NT molecule that has received most attention. Chemical synapses that release ACh are known as cholinergic synapse. At the cholinergic synapse pre and post Synaptic membrane are separated by a synaptic cleft that averages to 20 nm in width. Most of ACh in the pre SN is packaged within vesicles consisting of several thousands of ACh molecules. There may be million of such vesicles in a single pre SN membrane. The arrival of action potential in a pre SN causes depolarization due to influx of calcium ions via voltage regulated calcium channels. During the brief period, calcium ion flood into the axoplasma and triggers exocitosis to release ACh into synaptic cleft. The further release of ACh comes to halt by rapid removal of calcium ions by active transport mechanisms out of the cytoplasm to extra cellular fluid or into mitochondria or endoplasmic reticulum[1].

The modeling of above events will give quantification into biological process which has remained grossly descriptive. The events of pre SN cholinergic are diagrammatically depicted in Figure 2.

Queueing Model (M/M/s: FCFS/∞/∞): Let λ be the average rate at which the vesicles containing neurotransmitters arrive at presenaptic membrane, where there are s(>1) number of SNAPs(trafficking protein) and μ be the mean service rate of each of the SNAPs. The inter arrival time of vesicle and service time of exocitosis follows an exponential distribution. Vesicles come from an infinite population and the capacity of presenaptic terminal is also infinite. The order of exocitosis is First Come First Serve. M in the queueing model indicates the Markovian property of exponential distribution. Then the probability of having n number of vesicles at any indefinite time is given by

$$P_n = \frac{\rho^n}{n!}\frac{1}{\frac{\rho^s}{s!(1-\rho/s)+\sum_{n=0}^{s-1}\rho^n/n!}}, n = 0,1,2,\ldots\ldots,(s-1), \quad (1)$$

$$= \frac{\rho^n}{s!s^{n-s}}\cdot\frac{1}{\frac{\rho^s}{s!(1-\rho/s)+\sum_{n=0}^{s-1}\rho^n/n!}}, n = s, s+1,\ldots\ldots\ldots \quad (2)$$

ρ<s, where ρ(=λ/μs) is the traffic intensity.

Equation (1) physiologically explains the release of NT from pre SN during Miniature End Plate Potentials (MEPPs), whereas, equation (2) explains the release of NT from pre SN during the Excitatory Post Synaptic Potentials (EPSPs).

The mean number of vesicles containing neurotransmitters waiting for exocitosis is given by,

$$L_q = \frac{\rho^s}{s!}\frac{\lambda\mu s}{(\mu s-\lambda)^2}\frac{1}{\frac{\rho^s}{s!(1-\rho/s)+\sum_{n=0}^{s-1}\rho^n/n!}} \quad (3)$$

When an impulse reaches the presynaptic terminal, there is a delay in time for exocitosis, given by

$$W_q = \frac{\rho^s}{s!}\frac{\mu s}{(\mu s-\lambda)^2}\frac{1}{\frac{\rho^s}{s!(1-\rho/s)+\sum_{n=0}^{s-1}\rho^n/n!}} \quad (4)$$

During action potential the available SNAPs are busy; whose expected number is the traffic intensity ρ. Also the probability of no arrival of NT in the synaptic cleft as it happens in poisoning by botulism toxin as depicted in figure 2b, is given by equation (5)

$$P_0 = \frac{1}{\frac{\rho^s}{s!(1-\rho/s)+\sum_{n=0}^{s-1}\rho^n/n!}} \qquad (5)$$

Discussion: The nervous system is unique in the vast complexity of thought processes and control actions it can perform. It literally receives millions of information from variety of sensory nerves and integrates to determine the appropriate responses. Very fundamental to these is neuro transmission, communication between the neurons. The chemical NT which has solely remain descriptive need to be quantified. The quantification of this complex phenomenon requires application of mathematical consequences like the queueing model described above. The characteristic feature of chemical synapse of unidirectional flow is appropriately fits the queueing model. Here the regulation of neuro transmission is achieved by various exponential and critical factors like vast amount of NT released and critical controls like snapse. The neuro physiology has remained black box in the area of quantitave aspects of neuro transmission. In diseases like Myasthenia Gravis (MG) where defect is in the neuro transmission of cholienergic synapse leads to weakness of the muscles. The amplitude of the compound muscle action potential (CMAP) elicited by repetitive nerve stimulation (RNS) is normal or only slightly reduced in patients without MG. The amplitude of the fourth or fifth response to a train of low frequency nerve stimuli falls at least 10% from the initial value in myasthenic patients. This decrementing response to RNS is seen more often in proximal muscles, such as the facial muscles, biceps, deltoid, and trapezius than in hand muscles. A significant decrement to RNS in either a hand or shoulder muscle is found in about 60% of patients with Myasthenia Gravis[2]. The effective sustained neuro transmission is an output of series of actions like degradation of ACh, transport of choline into the pre SN, synthesis of ACh, filling of ACh into the vesicles and ultimately release of ACh into the synaptic cleft. In our model we have highlighted the role of several physiological limiting factors and try to model them. So in a hope, a better understanding of the neuro transmission could throw light, why the amplitude of RNS falls to low frequency in MG patients.

REFERENCES

1. Guyton, A.C., J.E. Hall, 2006. Textbook of Medical Physiology, 11th Ed, Elsevier, Singapore, 555-584.
2. Husain, A.M., Massey J.M., Howard J.F., Sanders DB, 1998. Acetylcholine receptor antibody measurements in acquired myasthenia gravis. Diagnostic sensitivity and predictive value for thymoma., Ann N Y Acad Sci., 13,841: 471-4.
3. Gross, D., Harris C.M., 2004. Fundamentals of Queueing Theory, John Wiley, 3rd ed, 69-74.