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SHORT-TERM SYNAPTIC PLASTICITY

Robert S. Zucker

Department of Physiology-Anatomy, University of California, Berkeley, California 94720

INTRODUCTION

Chemical synapses are not static. Postsynaptic potentials (PSPs) wax and wane, depending on the recent history of presynaptic activity. At some synapses PSPs grow during repetitive stimulation to many times the size of an isolated PSP. When this growth occurs within one second or less, and decays after a tetanus equally rapidly, it is called *synaptic facilitation*. A gradual rise of PSP amplitude during tens of seconds of stimulation is called *potentiation*; its slow decay after stimulation is *post-tetanic potentiation* (PTP). Enhanced synaptic transmission with an intermediate lifetime of a few seconds is sometimes called *augmentation*. Potentiated responses lasting for hours or days are called *long-term potentiation*. This latter process, not usually regarded as short-term, is the subject of a separate review (Brown et al 1989, this volume).

Other chemical synapses are subject to fatigue or depression. Sustained presynaptic activity results in a progressive decline in PSP amplitude. Most synapses display a mixture of these dynamic characteristics (Figure 1). During a tetanus, or train of action potentials, transmission may rise briefly due to facilitation before it is overwhelmed by depression (Hubbard 1963). If depression is not too severe, augmentation and potentiation lead to a partial recovery of transmission during the tetanus. Following the tetanus, facilitation decays rapidly, leaving depressed responses which recover to the potentiated level, causing what appears as a delayed post-tetanic potentiation (Magleby 1973b). Finally, PTP decays and PSPs return to the same amplitude as that elicited by an isolated presynaptic spike.

Short-term synaptic plasticity often determines the information pro-

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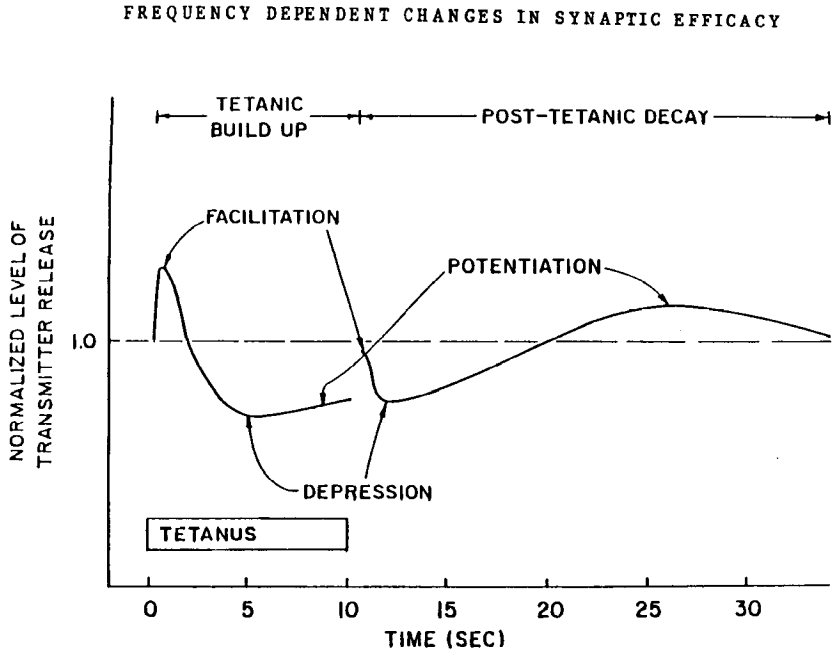

Figure 1 The effects of simultaneous facilitation, depression, and potentiation on transmitter release by each spike in a tetanus, and by single spikes as a function of time after the end of the tetanus.

cessing and response molding functions of neural circuits. In fish and insects, synaptic depression in visual and auditory pathways causes sensory adaptation and alteration in receptive fields of higher order sensory cells (O'Shea & Rowell 1976, Furukawa et al 1982). In *Aplysia*, depression at sensory to motor neuron synapses is responsible for habituation of gill withdrawal responses (Castellucci et al 1970). Synaptic depression at sensory terminals in fish, crustacea, and insects leads to habituation of escape responses to repeated stimuli (Auerbach & Bennett 1969, Zucker 1972, Zilber-Gachelin & Chartier 1973). And neuromuscular depression can weaken responses such as tail flicks in crayfish (Larimer et al 1971). In contrast, highly facilitating synapses respond effectively only to high frequency inputs. This shapes the frequency response characteristic of mammalian neurosecretory and sympathetic neurons and crustacean and amphibian peripheral synapses (Bittner 1968, Landau & Lass 1973, Dutton & Dyball 1979, Birks et al 1981). The important integrative consequences of synaptic plasticity motivate efforts to understand the underlying physiological mechanisms.

SYNAPTIC DEPRESSION

At some synapses depression is the dominant effect of repetitive stimulation. Quantal analysis at neuromuscular junctions demonstrates that depression is due to a presynaptic reduction in the number of quanta of transmitter released by impulses (Del Castillo & Katz 1954). Depression can often be relieved by reducing the level of transmitter release, for example by reducing the external calcium concentration or adding magnesium to block calcium influx at the nerve terminal (Thies 1965). The dependence of depression on initial level of transmission suggests that it is due to a limited store of releasable transmitter, which is depleted by a train of stimuli and not instantaneously replenished. Development of depression during a train and subsequent recovery are roughly exponential (Takeuchi 1958, Mallart & Martin 1968, Betz 1970), suggesting a first order process for renewing the releasable store within seconds.

Depletion Model

These characteristics of depression are consistent with a simple model (Figure 2) which has each action potential liberating a constant fraction of an immediately releasable store with subsequent refilling (or mobilization of replacement quanta) from a larger depot (Liley & North 1953). Only minor deviations from the predictions of this model have been observed:

1. The fraction of the store released by each impulse, as indicated by the fractional reduction in successive PSP amplitudes during a tetanus, may decline during depression (Betz 1970). Perhaps the most easily released quanta are secreted first, while those remaining are less easily released.
2. Depression in a train of impulses may be less severe than predicted from the decline of the first few PSPs (Kusano & Landau 1975), suggesting that replenishment of the releasable store is boosted (subject to extra nonlinear mobilization) by excessive release of transmitter.
3. Stimulation for several minutes often results in a second slow phase

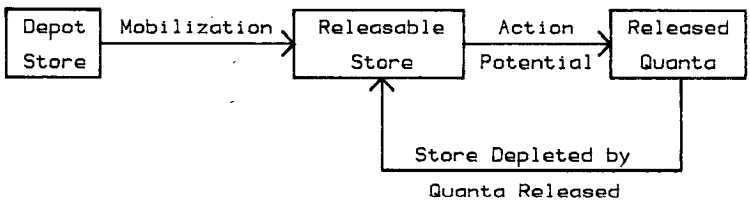

Figure 2 The depletion model of synaptic depression.

of depression (Birks & MacIntosh 1961, Elmqvist & Quastel 1965, Rosenthal 1969, Lass et al 1973), from which recovery also requires minutes. This may represent gradual depletion of the depot store of transmitter from which releasable quanta are mobilized.

One might expect the store of releasable quanta of transmitter to correspond to synaptic vesicles, or perhaps to those near the presynaptic membrane at release sites. However, synaptic depression develops faster and exceeds the reduction in vesicle number (Ceccarelli & Hurlbut 1980), leaving still unclear the identification of the structural correlate of the releasable store.

Release Statistics

Transmitter release is a statistical process, in which a variable number of quanta are released by repeated action potentials (Martin 1966). The quantal number is usually well described as a binomial random variable, characterized by n releasable quanta, each secreted by a spike with probability p (Johnson & Wernig 1971, Bennett & Florin 1974, McLachlan 1975a, Miyamoto 1975, Wernig 1975, Furukawa et al 1978, Korn et al 1982). Synaptic depression is sometimes associated with a drop in p (McLachlan 1975b, Korn et al 1982, 1984), but more often with a drop in n (Barrett & Stevens 1972a, Bennett & Florin 1974, McLachlan 1975b, Furukawa & Matsuura 1978, Glavinović 1979, Smith 1983).

Interpretation of these results depends on the physiological or structural meaning assigned to the parameters n and p. In one view (Bennett & Fisher 1977, Glavinović 1979), n is thought to be a measure of the releasable store of quanta, and p the fraction of this store released by a spike. Then reduction in n would be expected if depression is due to depletion of the releasable store. However, since n would then be reduced by depletion after each action potential, and would recover by mobilization from the depot store in the interval until the next spike, n itself would be a fluctuating random variable, and would not correspond to n of binomial release statistics (Vere-Jones 1966).

In another view (Zucker 1973, Wernig 1975, Bennett & Lavidis 1979, Furukawa et al 1982, Korn et al 1982, Neale et al 1983, Smith 1983), binomial release statistics are thought to arise from a fixed number of release sites (n), whereas p is the probability that a site releases a quantum. This notion is based on a correspondence between n and the number of morphological release sites observed at the same synapse. In this view, the store of releasable quanta corresponds to the fraction of release sites loaded with a quantum (probably a vesicle—see Oorschot & Jones 1987). This fraction drops during depletion, whereas n remains constant. The

probability p that a release site releases a quantum depends both on its probability of being filled (p_f) and its probability of being activated by an action potential (p_a) (Zucker 1973), according to $p = p_f p_a$. The binomial parameter p would then be less than the fraction of the releasable store activated by a spike, p_a. This has been observed experimentally (Christensen & Martin 1970). And only p should drop during depression.

Although appealing, this simple view is not supported by evidence cited above that depression is often accompanied by a reduction in n. This discrepancy may arise in part from the assumptions underlying the estimation of n and p. In particular, p is assumed to be uniform across release sites (or releasable quanta). This is an extremely unlikely assumption, and is actually controverted by experimental evidence (Hatt & Smith 1976b, Bennett & Lavidis 1979, Jack et al 1981). Moreover, any variance in p causes overestimation of average p, underestimation of n, and real changes in the values of p to be mirrored or even overshadowed by apparent changes in n (Zucker 1973, Brown et al 1976, Barton & Cohen 1977). These and other considerations (Zucker 1977) make accurate estimation of n and p, and their direct association with structures or physiological processes, difficult at best. Thus reductions in n are often thought to be loosely associated with a reduction in the proportion of release sites effectively activated by an action potential (Furukawa et al 1982, Smith 1983), due either to a depletion of quanta available to load the sites, or reduced activation of sites by partially blocked action potentials. The latter mechanism, although not usually a prominent factor in synaptic depression, has been found to be important during prolonged stimulation at some crustacean neuromuscular junctions (Parnas 1972, Hatt & Smith 1976a).

Other Mechanisms

At some central and peripheral synapses, depression is less dependent on the level of transmission and develops with a different time course during a tetanus than predicted by depletion models (Zucker & Bruner 1977, Byrne 1982). In *Aplysia*, habituation of gill withdrawal is due to presynaptically generated depression at synapses formed by sensory neurons (Castellucci & Kandel 1974). This depression is temporally correlated with a long-lasting inactivation of presynaptic calcium current measured in the cell body (Klein et al 1980). A similar correlation has been observed at synapses between cultured spinal cord neurons (Jia & Nelson 1986). This contrasts sharply with the squid giant synapse, where synaptic depression occurs in the clear absence of calcium current inactivation (Charlton et al 1982). A recent analysis indicates that this inactivation in *Aplysia* is insufficient to account for synaptic depression. A new model (Gingrich

& Byrne 1985) proposes that transmitter depletion also contributes to depression, and postulates a calcium-dependent mobilization of transmitter to counterbalance the change in transmitter release. This could result in the independence of short-term depression of the level of transmission when calcium levels are altered.

A long-lasting form of depression at these synapses underlies the long-lasting gill withdrawal habituation to trials of stimuli repeated for several days (Castellucci et al 1978). This depression is accompanied by a reduction in number and size of transmitter release sites and the number of synaptic vesicles each contains (Bailey & Chen 1983). How short-term depression is consolidated into long-lasting morphological changes is still unknown.

Although depression normally involves only a reduction in the number of quanta released, prolonged stimulation at central synapses in fishes and at neuromuscular junctions in frogs results also in a reduction in the size of quanta released (Bennett et al 1975, Glavinović 1987). It appears that after releasable vesicles or activated release sites are strongly depleted, reloaded sites or newly formed vesicles are not entirely refilled between stimuli in a tetanus.

Finally, at some multi-action synapses, depression arises from postsynaptic desensitization of neurotransmitter receptors. In *Aplysia*, a cholinergic interneuron in the abdominal ganglion binds to excitatory and inhibitory receptors on a motoneuron to elicit a diphasic excitatory-inhibitory PSP. The excitatory receptor is subject to desensitization, so that repeated activation results in a brief excitation followed by tonic inhibition (Wachtel & Kandel 1971). Iontophoresing acetylcholine onto the postsynaptic cell has the same effect. Just the opposite situation is seen at a buccal ganglion synapse. Here it is the inhibitory cholinergic receptors that are subject to desensitization, so that the synaptic effect changes from inhibition to excitation during repeated activation (Gardner & Kandel 1977).

These examples illustrate the multifaceted nature of *short-term depression*, caused by a variety of physiological processes at different synapses, and often having interesting consequences for information processing and behavior. A more prolonged form of depression, called *long-term depression*, is treated in a separate chapter (Ito 1989).

FACILITATION AND AUGMENTATION

Most synapses display a short-term facilitation, in which successive spikes at high frequency evoke PSPs of increasing amplitude. Depression may mask facilitation, which will then be evident only when depression is relieved by reducing the amount of transmitter released by spikes. At

numerous synapses, a quantal analysis indicates that facilitation is presynaptic in origin, reflecting increasing numbers of transmitter quanta released per spike (reviewed in Zucker 1973).

Early Theories of Facilitation

Early theories of facilitation invoked increased spike invasion of presynaptic terminals or effects of afterpotentials in nerve terminals (for reviews see Atwood 1976, Zucker 1977, Atwood & Wojtowicz 1986). The operation of such mechanisms has been refuted at central neurons (Charlton & Bittner 1978), peripheral neurons (Martin & Pilar 1964), and neuromuscular junctions (Hubbard 1963, Braun & Schmidt 1966, Zucker 1974a,c). Another hypothesis holds that spike broadening in nerve terminals, due to inactivation of potassium currents (Aldrich et al 1979), causes facilitation by increasing the calcium influx to successive action potentials (Gainer 1978, Andrew & Dudek 1985, Cooke 1985). Surprisingly, however, spike broadening in molluscan neurons is not accompanied by a measurable increase in calcium influx (Smith & Zucker 1980), and it is not involved in facilitation at crayfish neuromuscular junctions (Zucker & Lara-Estrella 1979, Bittner & Baxter 1983). Finally, synaptic facilitation could arise from a facilitated activation of calcium channels (Zucker 1974b), as has been observed in chromaffin cells (Hoshi et al 1984). However, calcium channels in *Aplysia* neurons (Smith & Zucker 1980) and at presynaptic terminals of squid synapses (Charlton et al 1982) exhibit no such facilitation to repeated depolarization.

Residual Calcium Hypothesis

At present, the residual calcium hypothesis of Katz & Miledi (Katz & Miledi 1968, Miledi & Thies 1971, H. Parnas et al 1982) enjoys the greatest popularity among synaptic physiologists. They propose that facilitation is the natural consequence of a nonlinear dependence of transmitter release upon intracellular calcium activity and the probability that after a presynaptic action potential some residual calcium will persist at sites of transmitter release (Figure 3).

To be more specific, transmitter release varies with about the fourth power of external calcium concentration at several synapses (Dodge & Rahamimoff 1967, Hubbard et al 1968, Katz & Miledi 1970, Dudel 1981). It has been argued that this measure will underestimate the cooperativity of calcium action (Parnas & Segel 1981, Barton et al 1983), so we will assume that transmitter release is determined by the fifth power of calcium concentration at release sites. Perhaps vesicle exocytosis requires the binding of several calcium ions to sites on the vesicular or plasma membrane.

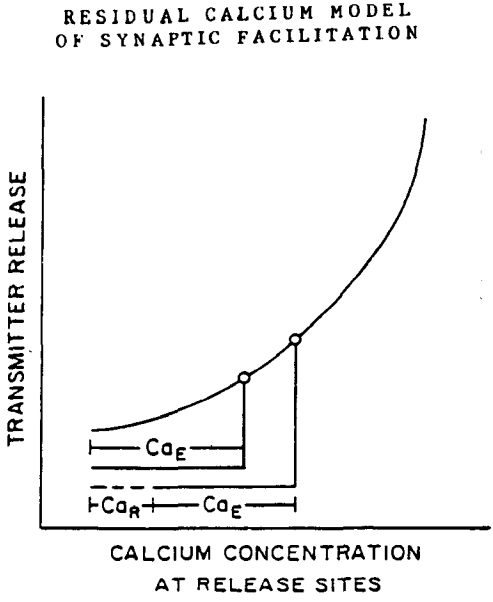

Figure 3 The residual calcium model of synaptic facilitation. Calcium entering in a spike (Ca_E) summates with residual calcium from prior activity (Ca_R) to release more transmitter than in the absence of prior activity. The nonlinear dependence of release on calcium causes Ca_R alone to release little transmitter.

Let the peak calcium concentration at release sites reach one unit during an action potential. Imagine that 10 ms later the calcium concentration has dropped to 0.05 unit. This residual calcium should release transmitter at a rate of $(0.05)^5$ or one three-millionth the rate of transmitter release during the spike. At frog neuromuscular junctions in low calcium solution, a spike releases about 1 quantum in 1 ms, so the residual calcium 10 ms after the spike should increase spontaneous release about 3×10^{-7} times 1000/s, or about 1 quantum/hr. A second action potential at this time will generate a peak calcium concentration at release sites of 1.05, which when raised to the fifth power will release 28% more quanta than did the first spike. Once having worked through such calculations, it is difficult to imagine that residual calcium would not lead to facilitation in this way.

Experimental Support

Calculations like those in the preceding paragraph show that after a tetanus in which residual calcium at release sites may reach 20% of its peak in the first spike, a facilitation of 660% will occur in the presence of an acceleration of miniature PSP frequency (spontaneous release of quanta) of

31/s. Such a correlation between facilitation of PSP amplitude and increase in miniature PSP frequency has been observed in several (Miledi & Thies 1971, Barrett & Stevens 1972b, Zucker & Lara-Estrella 1983) experiments using brief tetani. When the normal calcium gradient across the presynaptic membrane is reversed by removing all extracellular calcium, similar tetani cause a fall in miniature PSP frequency, presumably because of a drop in internal calcium as calcium exits through open calcium channels (Erulkar & Rahamimoff 1978).

The residual calcium hypothesis receives more direct support from three other sets of experiments:

1. Calcium is required for facilitation: Katz & Miledi (1968) showed that not only transmitter release but also facilitation requires calcium in the external medium. When they raised calcium after a conditioning impulse but before a test impulse, the first spike released no transmitter and also caused no facilitation of release to the second spike. One might conclude that the first spike must release transmitter in order to facilitate release to subsequent spikes. However, transmitter release fluctuates from spike to spike, and sometimes failures (releases of zero quanta) occur. Spikes releasing no transmitter cause as much facilitation as spikes that do release transmitter (Del Castillo & Katz 1954, Dudel & Kuffler 1961). Apparently, calcium entry during the first spike causes facilitation whether or not transmitter is released by the first spike.

2. Calcium elicits facilitation: Raising presynaptic calcium by fusing calcium-containing liposomes with presynaptic terminals (Rahamimoff et al 1978), poisoning calcium sequestering organelles (Alnaes & Rahamimoff 1975), or injecting calcium directly into terminals (Charlton et al 1982) facilitates transmitter release by action potentials.

3. Residual calcium accumulates during repeated activity: Calcium concentration in presynaptic terminals is seen to increase about ten-fold during a tetanus of 50 spikes, when it is measured spectrophotometrically with the indicator dye arsenazo III (Miledi & Parker 1981, Charlton et al 1982).

Residual Calcium Kinetics

Augmentation appears to be a longer lasting form of facilitation arising from similar mechanisms. It has been observed at neuromuscular junctions in frogs and synapses in sympathetic ganglia in rabbits, cerebral cortex in rats, and at central synapses in *Aplysia* (Magleby & Zengel 1976, Zengel et al 1980, Kretz et al 1982, Racine & Milgram 1983). A slow phase in increased miniature PSP frequency is also seen that corresponds to this phase of increased evoked transmitter release (Zengel & Magleby 1981). Like facilitation, augmentation requires calcium entry, since tetani in cal-

cium-free media do not elicit this increase in miniature PSP frequency of duration intermediate between facilitation and potentiation (Erulkar & Rahamimoff 1978).

The time course of the growth of facilitation and augmentation in a tetanus and its subsequent decline have received much attention. It was originally proposed that each impulse in a train added a constant increment of facilitation that decayed with two or more exponential components (Mallart & Martin 1967). This description is inadequate except for very brief tetani (Magleby 1973a, Linder 1974, Zucker 1974b, Bittner & Sewell 1976). A better fit to facilitation and augmentation is obtained by assuming that each impulse contributes an equal increment of residual calcium to a presynaptic compartment regulating transmitter release, that calcium is removed from this compartment by processes approximated as the sum of three exponentials (two for facilitation and one for augmentation), and that transmitter release is proportional to the fourth or higher power of calcium concentration in this compartment (Zengel & Magleby 1982).

Physical Models of Residual Calcium Kinetics

Recent attempts have been made to formulate physical models to explain the magnitude and time course of residual calcium at release sites necessary to account for facilitation and augmentation. Calcium crosses the presynaptic membrane into nerve terminals during action potentials (Llinás et al 1981, 1982) and acts at the surface to release transmitter. Calcium is bound to axoplasmic proteins (Alemà et al 1973, Brinley 1978) and diffuses toward the interior of the terminal after each spike, where it can no longer affect transmitter release. Finally, calcium is taken up into organelles (Blaustein et al 1978) and extruded by surface membrane pumps (Requena & Mullins 1979, I. Parnas et al 1982). The diffusion equation may be solved in cylindrical coordinates with boundary conditions imposed by measured rates of influx, binding, uptake, and extrusion (Alemà et al 1973, Blaustein et al 1978, Brinley 1978, Requena & Mullins 1979) to predict the magnitude and time course of intracellular calcium gradients during and after nervous activity. Transmitter release may be calculated from a power-law dependence upon calcium concentration at release sites.

The first simulations of these physical constraints used a one-dimensional model of radial calcium diffusion away from the surface and assumed uniform calcium influx across the membrane (Zucker & Stockbridge 1983, Stockbridge & Moore 1984). The time course and magnitude of facilitation following one spike at squid giant synapses and frog neuromuscular junctions were predicted reasonably accurately, as well as the tetanic accumulation of calcium and its decay as measured spectrophotometrically and the time course of spike-evoked transmitter release as mea-

sured electrophysiologically (Zucker & Stockbridge 1983, Fogelson & Zucker 1985). However, these simulations predicted too high a post-tetanic residual calcium compared to peak submembrane calcium in a single spike (Fogelson & Zucker 1985).

This defect was remedied in a subsequent model (Fogelson & Zucker 1985) in which calcium enters through an array of discrete channels and releases transmitter from release sites near these channels. The brief synaptic delay from calcium influx to transmitter release (0.2 ms) requires that transmitter release occur near calcium channels before calcium equilibrates at the surface (Simon & Llinás 1985), when distinct clouds of calcium ions still surround each open channel. After a spike, calcium diffuses in three dimensions away from each channel, and away from the clusters of channels, vesicles, and release sites called *active zones* (Pumplin et al 1981). The peak calcium concentration at release sites in active zones in such a model is much higher than in the simpler, one-dimensional diffusion model, and even after a tetanus the residual calcium never reaches this level. Simulations using this model provide a quantitatively better, although still imperfect, fit to data on phasic transmitter release, accumulation of presynaptic calcium, and facilitation and augementation at squid synapses and neuromuscular junctions.

These simulations demonstrate that diffusion of calcium away from release sites will resemble a multi-exponential time course. This is because diffusion follows a second-order differential equation. Therefore, the existence of multiple exponentials in descriptions of the kinetics of facilitation and augmentation does not indicate that these necessarily reflect independent processes. Changes in a single parameter, such as cytoplasmic calcium binding, have unequal effects on the different apparent exponential components of facilitation. However, it is true that changes in cytoplasmic binding affect mainly the fast process of facilitation through effects on diffusion, whereas changes in calcium uptake or extrusion affect mainly the slower process of augmentation in these simulations. Substituting strontium for calcium prolongs mainly the slow component of facilitation, while addition of barium accentuates augmentation (Zengel & Magleby 1980). It is possible that strontium binds differently than calcium to cytoplasmic proteins, while barium interferes with extrusion or uptake pumps.

Release Statistics

As with synaptic depression, facilitation and potentiation are accompanied by changes in the binomial release parameters n and p. In different preparations, apparent increases are observed mainly in p (Zucker 1973, Hirst et al 1981), mainly in n (Bennett & Florin 1974, McLachlan 1975a,

Branisteanu et al 1976, Wojtowicz & Atwood 1986), and in both p and n (Wernig 1972, Smith 1983). These results are all consistent with transmitter release occurring at release sites with nonuniform probabilities of activation. Both facilitation and potentiation might cause release sites to be more effectively activated by spikes. Whether this will be expressed mainly as an increase in n or in p depends on the exact form of the distribution of the values of p among release sites.

POTENTIATION

Potentiation is an increase in efficacy of transmission requiring minutes for its development and decay at synapses in sympathetic ganglia, olfactory and hippocampal cortex, and *Aplysia* ganglia (Waziri et al 1969, Richards 1972, Magleby & Zengel 1975, Atwood 1976, Schlapfer et al 1976, Zengel et al 1980, Racine & Milgram 1983). At crustacean neuromuscular junctions, quantal analysis shows potentiation to be presynaptic in origin (Baxter et al 1985, Wojtowicz & Atwood 1986). Unlike facilitation and augmentation, post-tetanic potentiation decays more slowly following tetani of longer duration or higher frequency (Magleby & Zengel 1975, Schlapfer et al 1976).

Potentiation appears to arise from two sources. It is reduced but not abolished by stimulation in a calcium-free medium (Rosenthal 1969, Weinreich 1971, Erulkar & Rahamimoff 1978). This suggests that potentiation is partly due to slow phases of removal of calcium that entered through calcium channels. Perhaps calcium pumps become saturated, or energy stores are limiting, in high calcium loads. The decay of PTP resembles that of post-tetanic calcium-activated potassium current and spectrophotometrically measured presynaptic calcium activity in *Aplysia* neurons (Kretz et al 1982, Connor et al 1986), a finding again suggesting that PTP reflects a late component in removal of residual calcium. The existence of a transition temperature in the decay kinetics of PTP (Schlapfer et al 1975) and the influence of alcohol on this decay rate (Woodson et al 1976) suggest that potentiation depends on some membrane process, such as calcium uptake into endoplasmic reticulum or its extrusion by surface pumps.

At neuromuscular junctions, part of potentiation is independent of calcium entry during a tetanus. This part is enhanced by treatments that augment sodium loading of nerve terminals, such as blocking the sodium pump with ouabain, and is reduced when sodium loading is minimized in low sodium media (Birks & Cohen 1968a,b, Atwood 1976). Transmitter release can be potentiated by exposing junctions to sodium-containing liposomes (Rahamimoff et al 1978), introducing sodium with ionophores

(Meiri et al 1981, Atwood et al 1983), and injecting sodium into nerve terminals (Charlton & Atwood 1977, Wojtowicz & Atwood 1985). It has been proposed that sodium that accumulates presynaptically during a tetanus potentiates transmitter release by displacing calcium from intracellular stores (Rahamimoff et al 1980) or reducing calcium extrusion by Na/Ca exchange (Misler & Hurlbut 1983). Lithium and rubidium Ringers enhance potentiation, presumably by blocking Na/Ca exchange (Misler et al 1987).

These results suggest that potentiation might be viewed as another consequence of increased residual calcium, dependent in part upon sodium accumulation. However, if this were the whole story, potentiation would summate with facilitation and augmentation. When this point has been examined, however, the interaction of potentiation with facilitation has appeared more multiplicative than additive (Landau et al 1973, Magleby & Zengel 1982). This suggests that another site of action of presynaptic calcium may also be involved in potentiation (Figure 4). Recently, Llinás et al (1985) have found that a calcium-dependent phosphorylation of presynaptic synapsin I, a synaptic vesicle protein, can potentiate transmitter release. It is possible that a calcium-dependent mobilization of transmitter mediated by this protein plays a role in PTP.

CONCLUSION

This concludes my brief survey of processes involved in short-term synaptic plasticity. Synaptic efficacy is a highly plastic variable, subject to numerous

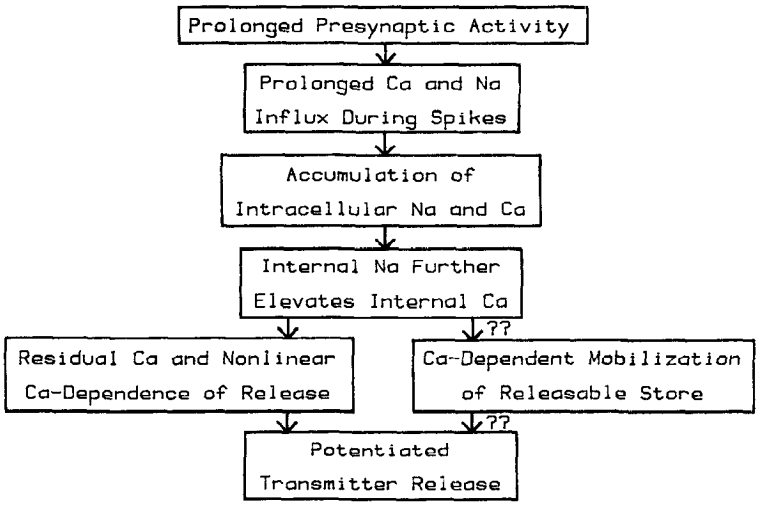

Figure 4 The sodium accumulation and secondary calcium action models of potentiation.

pre- and postsynaptic modulations affected by prior activity. These processes shape dramatically the pattern selectivity of synapses and the information transfer they mediate. Sensory phenomena such as adaptation and dynamic versus static sensitivity often arise from synaptic processes like depression and facilitation. These synaptic qualities are also expressed behaviorally as habituation and in the recruitment of elements in a pool of target neurons. Longer lasting processes such as long-term potentiation or depression build on these shorter processes to span the gap between synaptic plasticity and permanent structural changes involved in long-term memory. As processes providing clues to the basic mechanisms underlying synaptic transmission, the various forms of short-term synaptic plasticity promise to remain popular topics of intensive research.

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