Actomyosin-Like Protein in Brain

Actomyosin-like protein may function in the release of transmitter material at synaptic endings.

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Of the many events that occur at synaptic junctions the method by which transmitter material is released in response to stimulation is one of the least understood. Based on recent evidence of the disparate distribution of actin-like and myosin-like protein in brain subcellular fractions, a hypothesis is proposed that would explain such release by chemomechanical transduction at sites of interaction between presynaptic vesicles and membranes.

Calcium and Exocytosis

According to the present theory for the quantal release of acetylcholine at the neuromuscular junction, in response to a nerve impulse this transmitter is released from presynaptic vesicles in which it is stored (*1*). It was suggested by Katz and Miledi (*2*) that the influx of Ca^{2+} at the presynaptic junction in response to stimulation sets in motion a series of events that lead to the release of the transmitter material. This concept has been extended as being applicable to the release of other putative transmitter materials at other synaptic sites. The fact that acetylcholine is the immediate physiological stimulus to the chromaffin cells of the adrenal medulla for the release of adrenalin and noradrenalin led to the comparison of the "excitation-contraction coupling" in muscle with "stimulus-secretion coupling" in the adrenal gland (*3*). Here, too, the entrance of Ca^{2+} is a critical event as it is at the neuromuscular junction. In the adrenal medulla, the ratio of the released catecholamines to the simultaneously released adenosine triphosphate (ATP) and ATP metabolites is the same as the ratio in which these substances are found in the granules where they are stored (*4*). Molecules of large size, such as those of the enzyme that converts dopamine to norepinephrine, dopamine β-hydroxylase, and of the carrier protein, chromogranin A, are also released (*5*). Efflux of norepinephrine, dopamine β-hydroxylase, and chromogranin A from sympathetic nerve endings in the spleen after stimulation of the splenic nerve has also been demonstrated (*6*). Recently, it has been reported that stimulation of the hypogastric nerve causes a proportional release of norepinephrine and dopamine β-hydroxylase from the guinea pig vas deferens (*7*). The release of dopamine β-hydroxylase and norepinephrine at sympathetic nerve endings has also been shown to be activated by calcium (*8*). The efflux of these proteins along with transmitter material has strengthened the supposition that these materials are stored in vesicles from which they are released by exocytosis. It has been suggested that this release mechanism involves the fusion of the vesicle with the synaptic membrane leading to the opening of both sets of membranes and the extrusion of the vesicle contents. The membranes may then remain fused, or the vesicle may separate from the presynaptic site, close up, and be used again for the uptake and storage of transmitter material, or the vesicle may be metabolized and thus not be used in a recycling process.

Arguments for, as well as against, exocytosis being the process by which materials are released from vesicles have been reviewed extensively (*9*). Most investigators support the idea that exocytosis occurs, but do not agree on whether transmitter materials are released as a result of fusion of both sets of membranes or as a result of transient interactions between the membranes. The demonstration that the composition of the vesicular membrane is different from the composition of the synaptic membrane suggested that actual fusion of the vesicular membrane with synaptic membrane probably does not occur and that the vesicles probably do not arise from invagination of the synaptic membrane (*10*). Nevertheless, any mechanism that ascribes the release of transmitter from its store in the vesicle in response to stimuli must take into account the interaction of two sets of membranes that open to permit the exit of a regulated mixture of small as well as large molecules. This process of exocytosis could occur by a mechanochemical interaction between the vesicle and synaptic membrane with resultant conformational changes in the interacting membranes leading to extrusion of vesicle contents. The basic model for the conversion of chemical to mechanical energy is the actomyosin system of muscle. Hypotheses have been advanced that the molecular basis of exocytosis in the adrenal medulla and for the release of transmitters and secretory products in general involves a contractile event (*11*).

Actomyosin-Like Proteins

In recent years, contractile proteins similar to actomyosin have been isolated from a variety of nonmuscle tissues. They have been extracted from ascites sarcoma cells (*12*), blood platelets (*13*), adrenal medulla (*14*), and slime mold plasmodia (*15*). Actin-like protein has been purified from acanthamoeba (*16*) and sea urchin eggs (*17*); myosin-like protein has also been obtained from acanthamoeba (*18*). Actin-like protein has been demonstrated in sperm tails and meiotic spindles of the crane fly (*19*) and the mitotic spindle of locust testis (*20*). More important for this discussion is the isolation of actomyosin-like, actin-like, and myosin-like proteins from mammalian brain (*21*). These have been designated neurostenin, neurin, and stenin, respectively, to differentiate them from similar proteins from other sources. Furthermore, these studies

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have led to the isolation of actomyosin-like protein (neurostenin) from the synaptosomal subcellular fraction prepared from bovine and rat brains (*22*). Similar protein could not be isolated from purified mitchondrial, microsomal, myelin, or supernatant fractions; this gave credence to the supposition that the protein was isolated from structures associated with nerve endings. It should be noted that purified preparations of intact mitochondria and microsomes from brain do exhibit Mg^{2+},Ca^{2+}-stimulated adenosine triphophatse activity, but the properties of the mitochondrial and microsomal enzymes are not characteristic of actomyosin (*22*). Actin-like protein has now also been demonstrated to be present in cultures of chick sympathetic ganglia (*23*).

Properties of Neurostenin

Similar to actomyosin, the brain synaptosomal protein (*22*) is a Mg^{2+}, Ca^{2+}-activated adenosine triphosphatase that demonstrates both the phenomenon of superprecipitation in the presence of Mg^{2+} and ATP, and the viscosimetric sensitivity to ATP characteristic of such proteins. The protein was dissociated into actin-like (neurin) and myosin-like (stenin) protein by ultracentrifugation in sucrose gradients containing 0.6 molar potassium iodide and stabilized with 1 millimolar ATP. The neurin thus obtained, as well as muscle actin, stimulated the Mg^{2+}-activated adenosine triphosphatase activity of stenin and muscle myosin. The relative viscosities of mixtures of neurin with stenin, neurin with myosin, and actin with stenin were increased and became sensitive to added ATP; the addition of ATP to these mixtures resulted in a rapid decrease in viscosity which increased again as the ATP was hydrolyzed over a period of 30 to 60 minutes. Similar to actin, the neurin contains 3-methylhistidine and, similar to striated muscle myosin, stenin contains 3-methylhistidine and N^{ϵ}-methyllysine. Treatment with sodium dodecyl sulfonate and subsequent separation by means of electrophoresis on polyacrylamide gel indicate that the molecular weight of the neurin is approximately 47,000 and that the molecular weight of the major subunit of stenin is approximately 240,000; these values are close to those reported for actin and myosin, respectively. From 8 to 10 percent of the synaptosomal protein was isolated as neurostenin.

Vesicles and Membranes

In further studies of the distribution of these proteins in rat brain, the synaptosomal fraction was partially purified on a Ficoll gradient (*22*) and was then subjected to osmotic shock; in this way vesicular and membrane fractions were obtained (*24*). The vesicle and membrane pellets were suspended in ice-cold 0.05*M* tris(hydroxymethyl-aminomethane buffer (*p*H 7.2) containing 0.1 m*M* magnesium chloride and 1 percent (weight to volume) Triton X-100. The suspension was sonicated in an ice bath for two periods of 4 seconds each, a Branson Sonifier being used at an intensity of 5. Three volumes of Weber-Edsall solution (0.6*M* potassium chloride, 0.01*M* sodium bicarbonate, *p*H 9.2) was added and the mixture was homogenized in a glass homogenizer for 5 minutes at 0°C. After 18 hours at 4°C, the homogenate was centrifuged at 105,000*g* for 1 hour. The clear supernatant fluid was decanted and the *p*H adjusted to 6.3 by addition of ice-cold 0.125*M* sodium acetate buffer (*p*H 4.9). It was then dialyzed against four changes of approximately ten volumes of a solution of 0.05*M* tris, 0.06*M* KCl, and 0.04*M* sodium acetate (*p*H 6.3) over a period of 2 hours. The dialyzate was centrifuged for 30 minutes at 105,000*g* to collect the sedimenting protein.

The proteins thus obtained from the vesicle and membrane fractions were separately solubilized (3 to 5 milligrams per milliliter) in a solution of 0.05*M* tris, 1 m*M* ATP, 0.6*M* KI, and 0.04*M* sodium thiosulfate (*p*H 7.8) and layered onto a continuous sucrose gradient (3 to 30 percent, weight to volume) prepared in the same solution; the gradients were centrifuged at 4°C for 18 hours at 90,000*g* in an SW-25.1 rotor in the Spinco model L ultracentrifuge. Samples were collected from the bottom of the tubes in 2-milliliter fractions and, after dialysis to remove KI and sodium thiosulfate, were assayed for protein and adenosine triphosphatase activity. The Mg^{2+},Ca^{2+}-stimulated adenosine triphosphatase activity was measured by determination of the inorganic orthophosphate (P_i) released from ATP (*21*). The assays were carried out at 37°C in medium containing 0.03*M* imidazole-hydrochloride (*p*H 6.8), 0.06*M* KCl, 0.5 m*M* ATP, 0.1 m*M* ouabain, 1 m*M* Mg^{2+} or Ca^{2+}, with 0.01 to 0.05 mg of protein in a final volume of 1.0 ml. The reaction was terminated after 30 minutes by addition of 0.4 ml of 20 percent (weight to volume) trichloracetic acid.

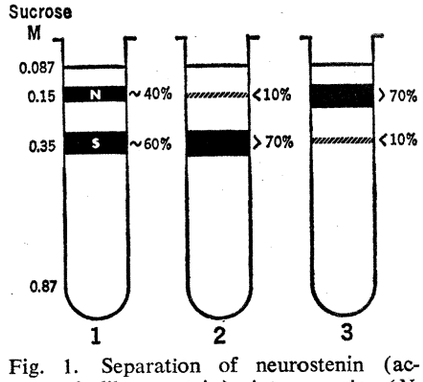

Fig. 1. Separation of neurostenin (actomyosin-like protein) into neurin (*N*, actin-like protein) and stenin (*S*, myosin-like protein) upon centrifugation in a continuous sucrose gradient. The gradient contained 0.6*M* KI, 0.04*M* sodium thiosulfate, 1 m*M* ATP, and 0.05*M* tris (*p*H 7.8). It was centrifuged at 4°C for 18 hours at 90,000*g* in an SW-25.1 rotor. Tube 1, protein isolated from rat brain synaptosomal preparation; tube 2, protein isolated from rat synaptic vesicle preparation; tube 3, protein isolated from rat synaptic membrane preparation.

Zonal centrifugation in sucrose gradients containing 0.6*M* KI caused the separation of neurostenin obtained either from whole brain (*21*) or from synaptosomal fractions (*22*) into two main protein bands (Fig. 1); the protein from one band manifested the properties of actin (neurin) and the protein from the other band, the properties of myosin (stenin). The former equilibrated at 0.15*M* sucrose and the latter at 0.35*M* sucrose. When the vesicular protein was subjected to centrifugation in sucrose gradients, only one major band appeared which centered at 0.35*M* sucrose (Fig. 1). In complementary fashion the centrifuged sucrose gradient of membrane protein showed one major band which centered at 0.15*M* sucrose. The vesicle protein was similar to the stenin isolated from either whole brain or synaptosomal neurostenin; it exhibited Ca^{2+}-stimulated adenosine triphosphatase activity and little Mg^{2+}-stimulated enzyme activity (Table 1). The membrane protein was similar to the neurin isolated from either whole brain or from synaptosomal neurostenin in that it demonstrated little enzyme activity alone but enhanced the Mg^{2+}-stimulated adenosine triphosphatase activity of the vesicle protein approximately five- to eightfold. The Mg^{2+}-stimulated adenosine triphosphatase activity of the vesicle protein was enhanced by muscle actin whereas the membrane protein had a

similar effect on muscle myosin (Table 2). Similar to the stenin isolated from whole brain or synaptosomal preparation, the protein isolated from the vesicle preparation also contained 3-methylhistidine and N^{ϵ}-methyllysine residues.

Any conclusions drawn from studies on protein distribution in subcellular fractions of brain must be tempered by the realization that such fractions are seldom pure. Electron microscopy of the fractions obtained by the procedure of De Robertis *et al.* (*24*) indicated that the membrane fraction was contaminated with myelin and mitochondrial fragments but with little, if any, vesicles. The vesicle preparation did contain what appeared to be small membrane fragments. Myelin and mitochondrial contamination were of little consequence since they were shown previously not to be a source of neurostenin (*22*). Because little stenin was obtained from the membrane fraction and, similarly, little neurin was extracted from the vesicle fraction, the results are interpreted as indicating that myosin-like protein may be associated with vesicles and actin-like protein with membranes. The contribution of other subcellular fragments that might have been present, such as glial cells, cannot be evaluated at this time.

Table 1. Effect of protein isolated from brain synaptosomal membrane fraction on the Ca^{2+}, Mg^{2+}-stimulated adenosine triphosphatase activity of protein isolated from the vesicle fraction. Results are expressed as micromoles of P_i per milligram of protein per minute. The incubation mixture contained 0.03*M* imidazole-HCl buffer (*p*H 6.8), 0.06*M* KCl, 0.5 m*M* ATP, 1 m*M* Mg^{2+} or Ca^{2+}, 0.1 m*M* ouabain, and either 0.01 mg of vesicle protein or 0.05 mg of membrane protein, or both, in a final volume of 1 ml. The enzymatic activity in the mixture was calculated on the basis of the amount of vesicle protein in the assay medium and corrected for the contribution of the membrane protein. Incubation time was 30 minutes at 37°C.

Vesicular protein		Membrane protein		Vesicle plus membrane proteins	
Ca^{2+}	Mg^{2+}	Ca^{2+}	Mg^{2+}	Ca^{2+}	Mg^{2+}
0.26	0.03	0.003	0.001	0.26	0.18
0.28	0.03	0.002	0.002	0.27	0.16
0.55	0.03	0.075	0.055	0.49	0.23

Neurostenin and Exocytosis

These studies and the studies on actomyosin-like protein isolated from brain synaptosomal fractions are the basis for the scheme presented in Fig. 2. In considering a mechanism by which release of transmitter substance at synaptic junctions may occur we suggest the possibility that at the site of contact between vesicles and presynaptic membranes, neurin and stenin combine to cause conformational changes in the membranes resulting in transient opening of the vesicle and the release of transmitter material into the synaptic cleft. After release of transmitter material the vesicle would separate from its synaptic site and either replenish its enzyme and transmitter complement and function in reuptake of transmitter material, or be metabolized. This sequence of events would be triggered by Ca^{2+} which is either released from binding sites in the membrane or enters the synaptic endings as a result of the depolarization that follows electrical stimulation. The action of Ca^{2+} and the hydrolysis of ATP during this process may have mechanistic similarities to that which occurs during muscle contraction. This integral role of Ca^{2+} is in keeping with the hypothesis of Katz and Miledi that depolarization at a presynaptic terminal causes an increase in the permeability of the terminal to Ca^{2+} which diffuses in and functions in transmitter release (*26*). Although the arrival of an action potential triggers the release of transmitter material, the release mechanism is independent of changes in sodium and potassium flux. Transmitter release, similar to many other secretory processes (*3*) is completely dependent on the presence of Ca^{2+} (*2*); it can occur in the absence of Na^{+} or when Na^{+} transport mechanisms are blocked. It has also been demonstrated that preganglionic stimulation increases Ca^{2+} uptake by sympathetic ganglia (*27*).

This hypothesis eliminates the requirement that during exocytosis the vesicle remains fused with synaptic membrane. Fusion would add considerable amounts of membrane to the synaptic surface during periods of sustained firing as well as cause a reduction in the number of vesicles. Although fusion has been observed in the superior cervical ganglia of the cat following prolonged supramaximal stimula-

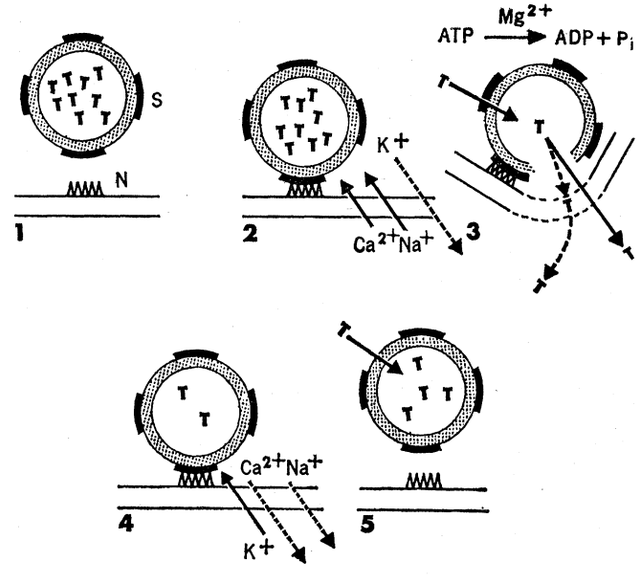

Fig. 2. Schematic diagram to explain release of transmitter material as a result of interaction between neurin (*N*) associated with synaptic membranes and stenin (*S*) associated with vesicle membranes. Stage 1, synaptic vesicle close to the presynaptic membrane. Stage 2, synaptic vesicle in intimate contact with the presynaptic membrane and the influx of Ca^{2+} in response to stimulation. Stage 3, the Ca^{2+} triggers interaction between neurin and stenin. Conformational changes in the membranes result in opening of the membranes. Transmitter (*T*) is released into the synaptic cleft or replaces transmitter in the membrane. Stage 4, the action is terminated by efflux of Ca^{2+}. Stage 5, the vesicle separates from the membrane.

tion (*28*) such observations may indicate that prolonged stimulation prevents the separation of vesicles from membranes which usually occurs under more normal physiological conditions. Evidence has also been presented that "fused" membrane is recycled for formation of synaptic vesicles at the frog neuromuscular junction (*29*). Other workers have failed to show any decrease in the total number of vesicles within a terminal under conditions during which release of transmitter should have been accelerated (*30*). In addition, studies on the turnover of protein in subcellular fractions of rat cerebral cortex (*31*) have underscored marked differences between synaptic vesicles and synaptic membrane. The former not only showed a relatively faster turnover (half-lives of 20 days as opposed to 44 days) but also had a higher initial specific radioactivity. These results were in agreement with previous observations on the half-life of phosphatidyl choline associated with various synaptic substructures (*32*). The results were thought to favor the interpretation that the synaptic vesicles are reused many times and that recycling takes place without fusion of the vesicle with the presynaptic membrane (*31*). Temporary junction rather than fusion is also suggested by freeze-fracture studies of cat spinal cord neuropil (*33*). The freeze-fracture technique reveals small depressions in the presynaptic membrane when the membrane is viewed from the inside. These depressions have been designated "synaptopores" and are thought to represent attachment sites of synaptic vesicles at the presynaptic membrane.

Whether or not the neurostenin system functions in the reuptake of materials may also be contemplated. Pinocytotic uptake into vesicles of the macromolecule, horseradish peroxidase, has been demonstrated at the lobster neuromuscular junction (*34*). The amount of uptake is increased upon electrical stimulation and it is of interest that optimal results were obtained in preparations in which periods of stimulation were alternated with periods of rest. One may also question whether the transmitter released from the vesicles empties directly into the synaptic cleft or into the synaptic membrane, replacing or displacing transmitter material held in the membrane. It is conceivable that released material is in equilibrium with that held in the membrane. In fact, it has been suggested that the active molecules are those of acetylcholine (*35, 35a*) or norepinephrine (*36*) stored in the membrane, rather than molecules of transmitter materials in the vesicle. Thus, three or four pools, or compartments, of transmitter materials may be postulated; (i) in the membrane, (ii) in the vesicles associated with synaptic membrane and ready for release, (iii) in vesicles further removed from the membrane and not in position for release, and (iv) perhaps in the cytoplasm. Acetylcholine, norepinephrine, and dopamine have each been shown to be concentrated in more than one site in nerve endings, and there appears to be a preferential release of newly synthesized substances (*35a, 37*). Similarly, in the adrenal medulla, about 20 percent of the catecholamines are usually found in extragranular fractions. It has been argued that it is the "free" catecholamines in the cytoplasm of the chromatin cells that form the pool from which catecholamines are released upon stimulation, while the vesicles serve as reserve storage sites (*38*). Thus, although it is generally accepted that transmitter material is directly released from presynaptic vesicles following nerve stimulation, the nature of the interactions among the postulated compartments of transmitter material requires further investigation.

Table 2. Ca^{2+},Mg^{2+}-stimulated adenosine triphosphatase activity of mixtures of vesicle protein with muscle actin, and membrane protein with muscle myosin. Results are expressed as micromoles of P_i per milligram of protein per minute. Assay conditions were as in Table 1.

Protein	Ca^{2+}	Mg^{2+}
Vesicle protein	0.49	0.037
Muscle actin	0.002	0.001
Vesicle protein and muscle actin	0.45	0.11
Membrane protein*	0.006	0.007
Muscle myosin	0.25	0.027
Membrane protein and muscle myosin	0.33	0.12

* Extracted directly from the synaptosomal membrane fraction (*25*).

It would be of great interest to know where in their respective structures actin- and myosin-like proteins are located. Is the myosin-like protein located in the vesicular membrane, or is it associated with the vesicular membrane at its exterior surface, or is it perhaps partially embedded in the membrane matrix? We do not know how many sites of stenin protein are associated with each vesicle. It may very well be that the hexagonally or pentagonally structured coat or "basket," which has been described as surrounding vesicles of nerve endings of brain (*39*) is the site of the concentration of stenin. The location of the actin-like protein also needs further clarification. It has been suggested that the actin-like protein may be associated with certain microfilaments in close proximity to plasma membrane in neurons and glia (*40*).

Alkaloids and Cytochalasins

There is a general hypothesis that contraction in a variety of cells, including neurons and glia, is associated with microfilaments which are disrupted by the fungal metabolite cytochalasin B (*40*). Cytochalasin B as well as the alkaloids, colchicine and vinblastine, inhibit the release of both dopamine β-hydroxylase and norepinephrine during stimulation of sympathetic nerves (*41*). Colchicine and vinblastine also inhibit the release of catecholamines from the adrenal medulla (*42*). The effect of colchicine and vinblastine on the release mechanism has been attributed to their interaction with microtubules. However, it has been reported that cytochalasin B causes a decrease in the viscosity of striated muscle actomyosin as well as inhibition of the adenosine triphosphatase activity of actomeromyosin (*43*). This complex is formed by the interaction of actin with heavy meromyosin, the latter protein is a major portion of myosin and retains the ability to interact with actin. The inhibitory action of cytochalasin B is thus thought to occur on the actin moiety of actomeromyosin. Studies in our laboratory indicate that these three drugs also inhibit in particular the Mg^{2+}-stimulated adenosine triphosphatase activity of neurostenin isolated from the synaptosomal fraction (*44*). This would also suggest that they react essentially with the actin-like moiety. It is interesting that Feit and Barondes (*45*) found particulate as well as soluble colchicine-binding material in brain. The particulate colchicine-binding material was associated with the microsomal and nerve-ending subfractions. These workers concluded, therefore, that the action of colchicine cannot necessarily be attributed directly to an effect on neurotubules. Similarly, vinblastine has been shown to precipitate, in addition to colchicine-binding protein, a variety of other proteins, including muscle actin (*46*) as well as the actin-like protein present in cultures of chick sympathetic

ganglia (*23*). We suggest that the action of these drugs on the storage and release of catecholamines may be mediated through an effect on the actomyosin-like system at the nerve endings. We have found that these drugs do affect the uptake, storage, and release of putative transmitter agents in isolated brain synaptosomal preparations (*44*). Furthermore, the recent report that deuterium oxide (D_2O) inhibits the coupling between excitation and contraction of the isolated muscle fibers of the barnacle by an inhibition of Ca^{2+} release (*47*) also allows one to question the interpretation of experiments with D_2O that microtubules might participate in the initial stimulated release of secretory or transmitter materials. The participation of microtubular structures in the release mechanism is partially predicated on the observations that D_2O, a "stabilizer" of microtubules, inhibits the glucose-stimulated release of insulin by pancreatic tissue (*48*) and enhances the nicotine-induced release of catecholamines from perfused adrenal gland (*42*). Because the release phenomenon in both tissues involves Ca^{2+} influx, D_2O might produce its initial effects by interacting with Ca^{2+} rather than affecting the microtubules in the tissues. The question of whether the actin in nerve endings is indeed associated with neurofilaments or is more closely associated with the membrane requires further investigation.

Transport of Vesicles

The site of formation of vesicles has received considerable attention. It is very probable that at least some of the vesicles are formed in the perikaryon and transported down the axon to the nerve endings along neurotubules (microtubules) (*49*). Myosin-like protein associated with vesicles would be just the protein to explain such transport (*50*). It is the counterpart to the demonstration that isolated microtubular protein does have actin-like properties (*51*). Microtubular protein prepared by the method of Weisenberg *et al.* (*52*) did enhance the Mg^{2+}-stimulated adenosine triphosphatase activity of muscle myosin and did increase the viscosity of muscle myosin and the viscometric sensitivity of the combination to added ATP (*51*). What has not been resolved is whether or not the isolated microtubular protein contained a small amount of actin-like protein.

Suggested Molecular Mechanism

In considering the type of reaction between neurin and stenin which might conceivably result in the opening of the vesicles for the exit of material, it is of interest to note that Dreizen and Gershman (*53*) have proposed the hypothesis that contraction of striated muscle involves a torsional movement of thick filaments within a rigid, thin filament lattice as a reasonable alternative to linear advance schemes based on independent cross-bridge interactions about a thick filament core. Although microfilamentous processes have been shown on occasion to be attached to neurotubules, cross-bridges similar to those between myosin and actin have not been demonstrated. A superficial consideration, which can only be offered because of lack of sufficient structural information, would suggest that a torsional interaction between stenin of vesicles and neurin of synaptosomal membranes could lead to the kind of conformation change in the vesicular membrane which would result in the opening of the membranes for the release of its contents. An analogy perhaps may be drawn to the opening of a key ring where a slight twist proves more efficient than a linear pull. The torsional distortion of the stenin would be expected to increase the helical conformation of the molecule. The action would be terminated simply by removal or binding of Ca^{2+} followed by a decrease in adenosine triphosphatase activity and consequent loss of torque force resulting in an uncoiling motion and the return of the stenin and neurin to their resting conformations.

Obviously other models may be proposed. The model presented here is intended only as a working hypothesis that can be approached experimentally and that at this time offers a molecular mechanism by which transient interaction between transmitter storage receptacles and synaptic membrane may lead to the release of transmitter material or their modifiers in response to synaptic activation.

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50. F. O. Schmitt has suggested that mechanochemical coupling similar to the contractile actomyosin muscle system may function in the flow of vesicles from the perikaryon down the axon to the nerve endings. He proposed a sliding vesicle model by which transport of vesicles via interaction with microtubules occurs; the principle is based on the sliding filament hypothesis of muscle contraction. See F. O. Schmitt, *Neurosci. Res. Program Bull.* **6** No. 2, 119 (1968).
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53. The model we present in this article is based on the reasoning of P. Dreizen and L. C. Gershman [*Trans. N.Y. Acad. Sci.* **32**, 170 (1970)]. These investigators believe that torsional distortion of the thick filament might be expected to be accompanied by the formation of weak enthalpic bonds, including hydrogen bonds, between groups along the helically arranged portions of myosin molecules. The torsional distortion would represent a low entropy state. The relaxation process would be driven by the gain in entropy as a result of uncoiling of the thick filament and possibly by repulsive coulombic forces between the negatively charged filaments consequent, in part, to ATP binding to myosin and actin, respectively.
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What's Wrong with Plastic Trees?

Rationales for preserving rare natural environments involve economic, societal, and political factors.

Martin H. Krieger

A tree's a tree. How many more [redwoods] do you need to look at? If you've seen one, you've seen them all.—Attributed to Ronald Reagan, then candidate for governor of California (*1*).

A tree is a tree, and when you've seen one redwood, given your general knowledge about trees, you have a pretty good idea of the characteristics of a redwood. Yet most people believe that when you've seen one, you haven't seen them all. Why is this so? What implications does this have for public policy in a world where resources are not scarce, but do have to be manufactured; where choice is always present; and where the competition for resources is becoming clearer and keener (*2; 3*, pp. 1–13)? In this article, I attempt to explore some of these issues, while trying to understand the reasons that are given, or might be given, for preserving certain natural environments (*4, 5*).

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The Ecology Movement

In the past few years, a movement concerned with the preservation and careful use of the natural environment in this country has grown substantially. This ecology movement, as I shall call it, is beginning to have genuine power in governmental decision-making and is becoming a link between certain government agencies and the publics to which they are responsible. The ecology movement should be distinguished from related movements concerned with the conservation and wise use of natural resources. The latter, ascendant in the United States during the first half of this century, were mostly concerned with making sure that natural resources and environments were used in a fashion that reflected their true worth to man. This resulted in a utilitarian conception of environments and in the adoption of means to partially preserve them—for example, cost-benefit analysis and policies of multiple use on federal lands.

The ecology movement is not necessarily committed to such policies. Noting the spoliation of the environment under the policies of the conservation movement, the ecology movement demands much greater concern about what is done to the environment, independently of how much it may cost. The ecology movement seeks to have man's environment valued in and of itself and thereby prevent its being traded off for the other benefits it offers to man.

It seems likely that the ecology movement will have to become more programmatic and responsive to compromise as it moves into more responsible and bureaucratic positions vis-à-vis governments and administrative agencies. As they now stand, the policies of the ecology movement may work against resource-conserving strategies designed to lead to the movement's desired ends in 20 or 30 years. Meier has said (*6*, p. 217):

The best hope, it seems now, is that the newly evolved ideologies will progress as social movements. A number of the major tenets of the belief system may then be