Figure 3 shows records taken simultaneously at 200, 107, and 42.5 kHz. The pulse lengths and beam widths at each frequency were nominally identical (0.1 msec, 5° by 10°). Since the three transceiver systems were not intercalibrated, direct comparison of signal levels is not possible. However, discrete scatterers (fish?) in the water column common to the three frequencies provide a basis for qualitative comparison of the relative signal levels at the three frequencies. The relative amplitude of the reverberation from the turbidity current to that from discrete scatterers decreases with decreasing frequency in these records. Since the median diameters of samples of sediment deposited along the channel axis are about 0.05 mm and that of the tailing before discharge is 0.03 mm, the median diameter of the particles suspended within the surge must be of the same order. This and the apparent frequency dependence of the signal suggest that the reverberation is due to Rayleigh scattering from suspended particles. The Rayleigh scattering mechanism has been suggested elsewhere (*3*) to account for reverberation from suspended sediment in the ocean and has been confirmed in additional quantitative experiments in Rupert Inlet in 1978 and 1979 (*4*).

A single-point mooring with two Aanderaa current meters set at a 2-minute sampling interval and at distances above the bottom of 3 and 13 m was in place during the event. The mooring location shown in Fig. 1 is approximate only, as we were unable to determine its exact position relative to the channel after deployment. The current records (Fig. 4) indicate a tidal modulation of a mean down-inlet flow. Subsequent to the onset of the event, there is an increase in vertical shear with higher up-inlet speeds (6 cm/sec) at the near-bottom meter and lower up-inlet speeds (< 2 cm/sec) at the upper meter. This shift to higher up-inlet speeds in the near-bottom zone suggests that the mooring was outside the channel.

The primary importance of the acoustic records in Figs. 2 and 3 lies partly in the fact that they represent the realization of a method for the remote detection of a phenomenon which subjects in situ instrumentation to high risk of loss or damage and partly in the fact that quantitative estimates of flow thickness, suspended solids concentration, and surge speed (from acoustic sounders distributed along the surge path) can be obtained (*4*). Theoretically, the surge speed along a horizontal bottom depends only upon the surge thickness and excess density due to suspended solids (*5*). Acoustic remote sensing offers the opportunity to test the theory on sloping bottoms at scales orders of magnitude greater than those achievable in the laboratory.

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Phosphorylation of Myosin Light Chains in Mouse Fast-Twitch Muscle Associated with Reduced Actomyosin Turnover Rate

Abstract. *Phosphorylation of the 18,000-dalton light chains of the fast-twitch myosin in mouse extensor digitorum longus muscles was correlated with reduction in the rate of the actomyosin adenosinetriphosphatase in vivo, but neither of these changes occurred in the soleus muscle. These results suggest that actomyosin interactions can be down-regulated by a reversible covalent modification of myosin light chains, that a mechanism for thick-filament regulation occurs in vertebrate skeletal muscle, and that the expression of this regulation may be limited to a specific fiber type.*

Myosin molecules contain lower molecular weight subunits called light chains (*1–3*). A functional role for light chains has been shown clearly (i) in systems where the primary control of contraction is linked to the myosin thick filament, such as in scallop muscle (*2–4*), or (ii) in smooth muscle where the expression of the regulatory nature of these light chains is dependent on their phosphorylation (*5–7*). In skeletal muscle, where the primary control of contraction is exerted on the actin-containing thin filament (*8*), a regulatory role of myosin light chains has not been established, since removal of these light chains from the parent molecule has little effect on its adenosinetriphosphatase activity in vitro (*9*). Nevertheless, vertebrate skeletal muscles contain the enzymes capable of reversibly phosphorylating the 18,000-dalton light chains (*10–12*). The possibility exists, therefore, that the expression of the regulatory nature of skeletal muscle light chains is linked to their phosphorylation. Yet, despite reports that light chain phosphorylation decreases the apparent K_m (K_m, Michaelis constant) for actin-activated myosin adenosinetriphosphatase in vitro (*13*) and that it is associated with post-tetanic potentiation of the twitch in rat fast-twitch muscle (*14*), no unified functional role has been demonstrated for myosin light chain phosphorylation.

Our experiments on isolated mouse muscles suggest phosphorylation of 18,000-dalton light chains is an unusual thick filament–linked regulatory system in that the modulation is inhibitory. The functional significance of phosphorylation of vertebrate skeletal muscle myosin may be related to the apparent fiber-type specificity. Fast glycolytic fibers are optimum for large power outputs (*15*) because of their large cross-sectional area and of their organization into large motor units. Maximum power is needed only in situations of extreme acceleration and of large power output. Fast-twitch fibers have a higher energy cost for contraction than do slow-twitch fibers (*16*). However, great speed and mechanical power is not necessary or useful for sustained forceful contractions. Phosphorylation of the light chains in these fibers and the concomitant reduction in actomyosin turnover rate may therefore be a mechanism to reduce fatigability in sustained forceful contractions.

We have previously reported a decrease in the rate of energy utilization

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Table 1. The relation between light chain phosphorylation and energy cost of contraction and maximum velocity of shortening in the mouse soleus and EDL. All measurements are expressed as means ± standard deviation. P_0 is the isometric tetanic force just before release or termination of stimulation. $\Delta \sim P_{init}$ and $\Delta \sim P_{rec}$ designate the extents of high-energy phosphate utilization during the periods of contraction and recovery, respectively (*16*), measured in micromoles of high energy phosphate per newton-meter-second. The maximum velocity of shortening, in fiber lengths per second, was measured from the velocity of unloaded shortening, V_{us} (*19*). LC2f-P/(LC2f-P + LC2f) represents the fractional extent of LC2f phosphorylation [data from (*17*)].

Tetanus duration (seconds)	P_0 (g)	$\Delta \sim P_{init}$	$\Delta \sim P_{rec}$	Maximum velocity of shortening	LC2f-P / (LC2f-P + LC2f)
			Soleus		
3	12 ± 1.3	9.1 ± 1.8	8.9 ± 0.4	1.88 ± 0.05	0.11 ± 0.05
9	11 ± 1.1	8.9 ± 1.9	8.7 ± 0.3	1.89 ± 0.04	0.12 ± 0.06
15	11 ± 0.6	8.8 ± 2.5	8.8 ± 0.3	1.88 ± 0.03	0.10 ± 0.05
			EDL		
3	17 ± 0.8	24.1 ± 3.6	22.1 ± 1.1	5.75 ± 0.13	0.22 ± 0.07
9	16 ± 1.2	14.8 ± 3.9	14.5 ± 1.9	4.07 ± 0.06	0.45 ± 0.06
15	13 ± 1.5	10.0 ± 1.2	11.4 ± 1.4	3.21 ± 0.10	0.51 ± 0.05

(*16*) and an increase in the extent of phosphorylation of the 18,000-dalton light chain of fast-twitch myosin (LC2f) (*17*) during a maintained tetanus of the fast-twitch extensor digitorum longus (EDL). None of these changes occurred in the slow-twitch soleus muscle. To test the hypothesis that phosphorylation of the 18,000-dalton light chain is a mechanism for down-regulation of actomyosin in fast-twitch muscle, we measured the maximal velocity of shortening after various durations of isometric tetanus. We now report a comparison of these mechanical data with the data on light chain phosphorylation and energetics. The muscles used were the isolated and intact slow-twitch soleus and fast-twitch EDL muscles of the mouse (*18*). The maximum velocity of shortening was estimated from the velocity of unloaded shortening (V_{us}) by the quick-release method (*19*).

The pattern of energy utilization for isometric contractions (*20*) differed in two respects in the mouse EDL and soleus muscles (*16*). (i) For short tetanuses, the initial rate of high-energy phosphate splitting during steady isometric contractions was about threefold higher in the EDL than in the soleus. (ii) With prolonged stimulation, this rate in the EDL subsequently decreased so that after 12 seconds of stimulation it had fallen to about half the initial rate. Comparable contractile activity induced no change in the rate of high-energy phosphate utilization in the soleus (Table 1). The reduction in the rate of energy utilization observed in the EDL followed a similar time course to that of LC2f phosphorylation (*21*) (closed squares in Fig. 1B). In the soleus there was no detectable change in either parameter (open squares in Fig. 1B). Throughout all these measurements, the tetanic force fell to not less than 80 percent of the initial force generation in EDL, and the fatigue of force was less in soleus (Table 1). This relative constancy of isometric force along with the reduction in the overall energy cost for tension maintenance suggested that LC2f phosphorylation is associated with a reduction in the actomyosin adenosinetriphosphatase rate in vivo. This suggestion is based on the assumption that a significant fraction of the reduction in whole muscle energy utilization is due to a reduction in the actomyosin adenosinetriphosphatase.

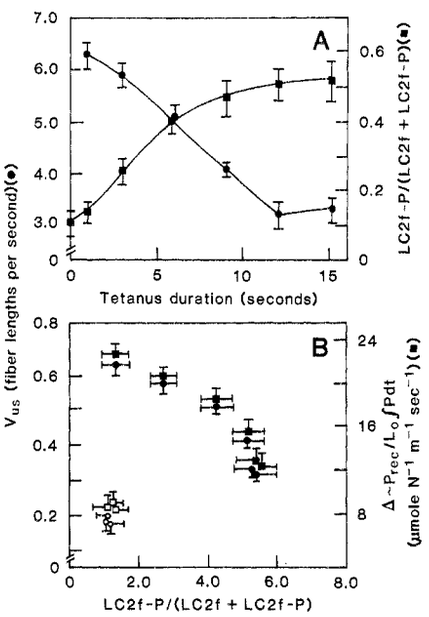

Fig. 1. The relation between LC2f phosphorylation (LC2f-P) and maximum velocity of shortening and reduction in total energy cost in the EDL. (A) The fractional extent of phosphorylation (■) and velocity of unloaded shortening, V_{us} (●), as a function of the tetanus duration in EDL. Each point represents the average of at least six muscles; bars represent 1 standard deviation. Phosphorylation data from (*17*). (B) The rate of energy utilization (□ and ■) and the maximum velocity of shortening (○ and ●) in the EDL (closed symbols) and in soleus (open symbols) as a function of the fractional extent of phosphorylation of LC2f. Each point represents the average of at least six muscles; bars represent 1 standard deviation. Data on energetics from (*16*). Only the points for unstimulated soleus and for a 9-second and 15-second tetanus of soleus are shown.

Measurement of the maximum velocity of shortening (V_{us}) as a function of the duration of the preceding tetanus provides a test of the hypothesis that the reduction in the energy cost of the EDL during prolonged stimulation is due, in part at least, to a reduction in the turnover rate of the actomyosin adenosinetriphosphatase. The values for V_{us} measured after various durations of isometric tetanus are given in Table 1. After a 1-second tetanus, the V_{us} of the EDL was approximately three times that of the soleus studied under comparable conditions. With prolonged stimulations, V_{us} in the EDL fell to approximately one-half its initial value. Neither brief nor prolonged stimulation induced any change in the velocity of shortening of the soleus.

Figure 1 also shows the relation between maximal velocity of shortening and the rate of energy utilization as a function of light chain phosphorylation. In the EDL, the parallel reductions in the rate of energy utilization and of V_{us} with continued stimulation were correlated with the extent of LC2f phosphorylation. In prolonged stimulations of the soleus, no change was observed in V_{us}, energy utilization, or in the extent of phosphorylation of either LC2f (data shown) or of the light chain of slow-twitch myosin (LC2s) (data not shown). Thus, there are distinctive qualitative differences between the fast-twitch EDL and slow-twitch soleus muscles with respect to LC2f phosphorylation, contractile energetics, and mechanics.

In control experiments, we tested the possibility that the energetic and mechanical changes were correlated with the extent of high energy phosphate splitting and product accumulation rather than with LC2f phosphorylation. In soleus, the depletion of phosphocreatine was much less in aerobic muscles than in anaerobic muscles (*16*), yet in neither case was there a change in velocity of shortening. The correlation between light chain phosphorylation and decrease in isometric energy cost and in velocity of shortening was unaltered in anaerobic or aerobic conditions in EDL. Light chain phosphorylation in EDL was independent of muscle lengths large anough to reduce isometric force tenfold (P_0, 0.6 P_0, and 0.1 P_0, where P_0 is the maximum

isometric force) with a concomitant threefold reduction in energy cost for a 9-second tetanus.

The effects of phosphorylation of LC2f in the mouse fast-twitch muscles differ in two major respects from the effects seen upon phosphorylation of smooth muscle light chains. (i) In mammalian skeletal muscles, the time course of phosphorylation occurs on a time scale at least two orders of magnitude slower than the contraction time (*16, 22*). (ii) Phosphorylation of the light chains in smooth muscle is associated with activation of the actomyosin adenosinetriphosphatase (*5, 6*) and is related to cross-bridge turnover rate (*23*), whereas our results indicate that phosphorylation of the light chains in vertebrate (mouse) skeletal muscles is associated with a reduction in the actomyosin adenosinetriphosphatase rate in vivo.

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21. Phosphorylation of the light chains of both fast- and slow-twitch myosin resulted in a shift in the isoelectric focusing point of the light chains toward the acidic region in two-dimensional gel electrophoresis as expected from the added negative charge. The identity of these spots as the phosphorylated derivative of the regulatory light chains was further tested by making autoradiograms of two-dimensional gels of muscles incubated for 8 hours in [^{32}P]orthophosphate so as to label the γ-phosphate of the adenosine triphosphate to a constant specific activity (*17*).
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Cardiovascular Actions of Cadmium at Environmental Exposure Levels

Abstract. *A low intake of dietary cadmium induces specific dose-dependent functional and biochemical changes in the cardiovascular tissues of rats. Maximum changes occur when the cadmium intake is 10 to 20 micrograms per kilogram of body weight per day. The changes reflect the accumulation of "critical" concentrations of cadmium in the cardiovascular tissues. The biologic activity of cadmium is demonstrated for intakes that approach those of the average American adult exposed to the usual environmental concentrations of the element but not to industrial concentrations. The sensitivity of the cardiovascular system to low doses of cadmium could not be anticipated by extrapolation from data on exposure to high concentrations of cadmium. The data support the hypothesis that ingested or inhaled environmental cadmium may contribute to essential hypertension in humans.*

Cadmium accumulates in human tissues as a direct function of age and level of exposure (*1, 2*). Geographic differences in the incidence of cardiovascular mortality have been directly correlated with cadmium concentrations in the environment (*3*). Despite this apparent association in humans, toxicologic indicators, for example, growth and hematologic characteristics in various animal models, are unaffected by exposure to cadmium at environmental levels (*4, 5*). (The average daily intake of cadmium in Americans and Europeans is 50 to 70 μg.) The generally accepted dose-response relations that have been formulated are based on these and similar experimental criteria (*2, 6*). Extrapolation from these dose-response curves has led to the prediction that in man cadmium is biologically inert when the intake range is 1 to 100 μg per day (*7*).

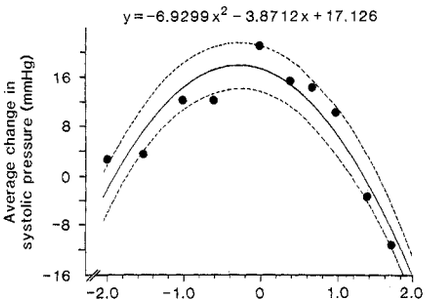

Fig. 1. Dose-effect curve depicting blood pressure difference relative to control after 18 months of exposure plotted against the logarithm of the cadmium concentration (0.01 to 50 ppm) in the drinking water. Each point represents the average of 16 or more rats per group, with a total population of 520 rats represented. The least squares equation for the curve which approximates this relation is shown and represented by the solid line. The dashed lines represent the standard deviation about the equation.

To test the validity of this prediction we have investigated the functional and metabolic effects of chronic low-level cadmium intake in rats, with emphasis on the cardiovascular system. Our results, which were not predicted from the accepted toxicologic dose-response relations, indicate that a cadmium intake of 10 to 20 μg per kilogram of body weight per day induces maximum cardiovascular changes. Ordinary environmental sources provide many members of industrialized societies with cadmium exposures in this range.

Weanling female Long-Evans rats were housed in a low-contamination environment and given free access to a rye-based low-cadmium diet and deionized water fortified with essential trace metals as described (*4*). Cadmium as the acetate salt was administered to the rats by way of the drinking water. Blood pressures were determined at quarterly intervals in triplicate by tail-cuff plethysmography in lightly anesthetized animals (25 mg of sodium pentobarbital per kilogram of body weight). Body weights were determined as an index of group well being. At 18 months, specific heart

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