Cross-bridge cycling theories cannot explain high-speed lengthening behavior in frog muscle

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ABSTRACT   The Huxley 1957 model of cross-bridge cycling accounts for the shortening force-velocity curve of striated muscle with great precision. For forced lengthening, however, the model diverges from experimental results. This paper examines whether it is possible to bring the model into better agreement with experiments, and if so what must be assumed about the mechanical capabilities of cross-bridges. Of particular interest is how introduction of a maximum allowable cross-bridge strain, as has been suggested by some experiments, affects the predictions of the model. Because some differences in the models are apparent only at high stretch velocities, we acquired new force-velocity data to permit a comparison with experiment. Using whole, isolated frog sartorius muscles at 2°C, we stretched active muscle at speeds up to and exceeding $2 V_{max}$. Force during stretch was always greater than the peak isometric level, even during the fastest stretches, and was approximately independent of velocity for stretches faster than 0.5 V_{max}. Although certain modifications to the model brought it into closer correspondence with the experiments, the accompanying requirements on cross-bridge extensibility were unreasonable. We suggest (both in this paper and the one that follows) that sarcomere inhomogeneities, which have been implicated in such phenomena as "tension creep" and "permanent extra tension," may also play an important role in determining the basic force-velocity characteristics of muscle.

INTRODUCTION

One of the great successes of A. F. Huxley's original cross-bridge cycling model (1957) is that, despite its intent to explain shortening results, it achieves qualitative agreement with experimentally measured force-velocity curves for lengthening muscle as well. For lengthening, the model predicts a change in slope of the force-velocity curve as it passes through the isometric condition ($V = 0$) and an asymptote in force at high lengthening velocities. Both of these have been widely reported in experimental work (see a summary in Woledge et al., 1985, p. 47). Whereas other cross-bridge models have been proposed to explain muscle phenomena such as high-speed transients and energy utilization (e.g., Huxley and Simmons, 1971; Julian et al., 1974; Hill et al., 1975; Eisenberg et al., 1980; Wood, 1981), none has improved on Huxley's basic cross-bridge cycling explanation of the macroscopic correspondence between force and velocity.

Based on this model, it is possible to draw certain conclusions about the mechanical characteristics of cross-bridges. Our primary goal is to examine what must be

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assumed about cross-bridges for the model to account correctly for forced lengthening results. Of particular interest is the notion that cross-bridges may have a maximum allowable strain, as suggested by some experimental results (Flitney and Hirst, 1978; Edman et al., 1978). We test this idea by adding a maximum strain condition to the Huxley model and comparing these predictions to experimental force-velocity data for high-speed stretches. It is shown that adding such a restriction to the model causes it to diverge rather severely from experimental results. The direct implication is that, as originally assumed in the model, cross-bridges have no clear limit of extension. The implausibility of this statement leads us to conclude that factors other than simple cross-bridge cycling dictate the shape of the force-velocity curve for lengthening. This is in contrast to shortening, in which cross-bridge cycling appears to be the predominant factor. Sarcomere inhomogeneity, a feature of striated muscle that very likely contributes to phenomena like tension "creep" (Julian et al., 1978) and "permanent extra tension" (Julian and Morgan, 1979), may also play a role in the more basic force-velocity relationship. This possibility is explored in the following paper.

Our approach in this work was to modify the Huxley model in an attempt to achieve quantitative, rather than qualitative, agreement with experimental force-velocity curves. In the original model, force generated during

lengthening exceeds 5 P_o (P_o = maximum isometric tension) for high-speed stretches. In experiments, force rarely exceeds half that amount and is usually below 2 P_o. Zahalak (1981) proposed a simple modification to the model, namely to increase the detachment rate for highly stretched cross-bridges, that brings the model into much closer agreement. Ward (1987) produced a model that incorporated a maximum cross-bridge strain, and we investigate here the addition of a nonlinearity to the cross-bridge stiffness.

The differences in the predictions of these modified cycling models are, in many cases, apparent only if the calculation includes high velocities of stretch. In slow stretching, for example, force-velocity data computed by the maximum strain model are nearly identical to those computed by the original Huxley model. It was important, therefore, to have reliable experimental data over a wide range (up to ~2 V_{max}) to make the necessary comparisons. Beginning with the first systematic experiments on stretches in active muscle (Katz, 1939), there have been a large number of investigations on the "negative side" of the force-velocity curve. Woledge et al. (1985, p. 71) have condensed the force-velocity results from several studies of slow lengthening behavior (Aubert, 1956; Curtin and Davies, 1973; Edman et al., 1978). Some data for stretching at moderate to high speeds have been reported by others (Joyce et al., 1969; Sugi, 1972; Flitney and Hirst, 1978; Colomo et al., 1988). Taken together, these investigations have in one form or another defined the lengthening force-velocity curve to speeds approaching V_{max}. There is, however, no one set of data that fulfills the requirements needed to permit a meaningful comparison to theoretical predictions of cross-bridge cycling. The requirements are (a) that the experiments be performed on frog muscle near 0°C, (b) that the muscle be in a steady state at the imposed velocity, and (c) that data be available at velocities approaching or exceeding 2 V_{max}. The Flitney and Hirst data, for example, span a fairly wide range of velocities but the measurements of force were made during, rather than after, an early transient that occurs just as the length change is initiated. The data of Colomo et al., while taken during steady state, do not extend beyond V_{max} in lengthening velocity. We performed a relatively simple set of force-velocity experiments on isolated, whole frog sartorius muscle at 2°C to obtain the required information.

METHODS

Whole muscle experiments

Muscle preparation

Small and medium-sized frogs (Rana pipiens) were obtained from a commercial supplier and kept in a large tank with running cold tap water; they were fed crickets weekly. The sartorius was dissected free from one leg leaving a small piece of pelvic bone attached to the proximal end. The distal tendon was firmly grasped in a series of knots of cotton suture. A total of 19 muscles were studied, the rest length and blotted mass of which were 26.4 ± 1.4 mm and 75.4 ± 18.4 mg (mean ± SD).

Apparatus

The muscle was suspended horizontally in a 2 × 2 × 8 cm plexiglass trough filled with saline (115.5 mM NaCl, 2.5 mM KCl, 1.8 mM CaCl$_2$, 0.85 mM NaH$_2$PO$_4$, 2.15 mM Na$_2$HPO$_4$, pH 7.0–7.1). The saline was maintained at 2 ± 1°C and oxygen was constantly bubbled into it. Muscle force was measured with a fixed transducer (model F5-1, Konigsberg Instruments, Inc., Pasadena, CA). This transducer with attachments had a natural frequency of 700 Hz in saline, a compliance of 0.0002 μm/N (manufacturer's specifications), and was calibrated before use by hanging a series of known weights from it. Muscle length was adjusted with a servo-controlled ergometer (model 305, Cambridge Technology, Inc., Watertown, MA). Step length changes could be completed in ~10 ms with no overshoot. The ergometer position sensor was calibrated with a dial micrometer. Force and position transducer signals were digitized at 2,000 samples/s on two channels of a digital oscilloscope (model 2090 with 201 plug-in, Nicolet Instrument Corp., Madison, WI). The oscilloscope, stimulator, and muscle length were controlled by a microcomputer (model Z-80 CP/M, Sierra Data Sciences, Fresno, CA). After each experiment, the force and length records were transferred digitally from the oscilloscope to the microcomputer for analysis.

Stimulation

Stimulation was delivered via 1 × 6 cm platinum plate electrodes placed 1 cm apart on either side of the muscle with 20–25 Hz, 14 V alternating polarity square waves of 1 ms duration. The output of the stimulator (model 6bp, modified for alternating polarity pulses, Frederick Haer & Co., Brunswick, ME) was amplified with an external high current unity gain amplifier (model PA07A, APEX Microtechnology, Tucson, AZ). The stimulation frequency of 20–25 Hz was the minimum required to maintain a fused tetanus; lower frequencies were sufficient for isometric tetani, but, as was noted by Joyce et al. (1969; Fig. 7), they could become unfused during stretching.

Experimental procedure

The twitch tension vs. length curve was determined for each muscle before the start of an experiment; the rest length (l_o) was selected as the length at which the muscle developed the greatest twitch tension. In separate control experiments, it was established that, at 2°C, l_o determined with twitches was the same as that determined with tetani. Each muscle was subjected to three different experimental protocols: (a) a 300-ms isometric tetanus at l_o; (b) a slack test from l_o + 2 mm of the sort described by Hill (1970, p. 42); and (c) one or more isovelocity stretches or releases. Each protocol was performed twice on each muscle, the group being organized into mirror pairs, i.e., symmetrically in time using a sequence such as a, b, c, c, b, a. The relevant data from the two halves of each pair were averaged. The first and last protocols were always isometric tetani, the second and penultimate were slack tests, with the isovelocity tests (from one to four pairs) constituting the inner pairs. For the 19 muscles studied, P_o was 0.55 ± 0.14 N (mean ± SD); V_{max} was 65.3 ± 7.1 mm/s.

The isovelocity stretch experiments were performed as follows. The isometric muscle was tetanically stimulated at l_o − 3.5 mm (l_o − 1.5 mm for very slow stretches) and then stretched at a constant rate to a length of l_o + 0.5 mm, at which time the stimulation was turned off. From the oscilloscope trace, force and velocity were measured as muscle

length passed through l_o. We corrected for parallel elasticity by digitally subtracting the force trace of an identical, unstimulated run. This never contributed >3% of the total force and was usually <1%. The magnitude of series elasticity was estimated from the amount of rapid recoil in the slack tests (56.9–147.1 dyn/μm; 111.8 ± 26.5 dyn/μm). This was used to compute the velocity of length changes actually imparted to the muscle. The average velocity correction was 1.1% V_{max}; the maximum correction was 10.3% V_{max}. Ramp velocities of −119 to +45 mm/s, corresponding approximately to −2.1–0.8 V_{max}, were studied (positive velocities correspond to shortening).

Mathematical models and computer simulations

Models of cross-bridge cycling

The Huxley 1957 model of cross-bridge cycling, and three modifications to it, were compared to the experimental results. The behavior of highly stretched cross-bridges were modified by (a) increasing their detachment rate (Zahalak, 1981), (b) forcing them to detach, i.e., infinite detachment rate, at a particular length (Ward, 1987), and/or (c) incorporating a nonlinear stiffness.

Computer simulations

Computer programs, written in the "C" language and run on an IBM-PC/AT computer, provided numerical solutions to the governing equations for the cross-bridge models. While other information was available from the simulations, we focused on the steady-state force-velocity predictions. The Zahalak parameter, g_3 (see Appendix), was varied over the range 0–70, and the maximum strain parameter, G, was varied from 2–6 (Gh is the maximum allowable strain). An arithmetic residual, calculated as the sum of the absolute values of the differences between experimental and theoretical results, formed the basis upon which to judge "goodness of fit." Due to the complexity of the expressions for force as a function of velocity, a minimization of residual in the sense of least squares was not practical.

While any form of nonlinearity in cross-bridge stiffness could be accommodated in the model, only those resulting in increased stiffness at longer lengths were investigated. Specifically, the relationship between force and cross-bridge length was presumed to be of the form

$$P_{cross\text{-}bridge} = k(x + \beta e^{\alpha x}),$$

where k is the cross-bridge stiffness and α and β are parameters specifying the severity of the nonlinearity. In cases where a combination of g_3 and G caused the model to underestimate the force at high velocities of stretch, α and β were adjusted in an attempt to bring the model into closer correspondence to the experimental results.

RESULTS

Experiments

The most important result from the experiments is that, during very high-speed lengthening (approaching and exceeding 2 V_{max}), force remains well above P_0 (Fig. 1; $n = 19$). The ratio P/P_0 is essentially constant (1.2–1.5) over a wide range for stretching velocities, $-2.2 \leq V/V_{max} \leq -0.5$. Except for the high-speed data, the other features of this force-velocity curve are familiar. For example, we measure a slope 3.9 times greater for slow
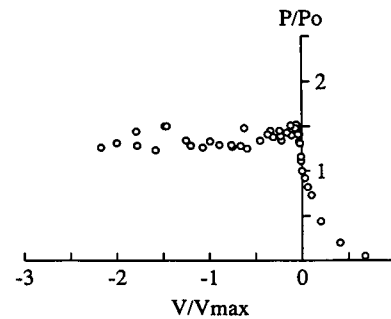

FIGURE 1 Force-velocity results for 19 muscles. Negative velocities correspond to stretches. A discontinuity in slope at $V = 0$ is apparent, as is the fact that yielding occurs for stretches faster than $\sim -0.1\ V_{max}$. The muscles continued to generate force greater than isometric ($P/P_0 > 1$) even when forced to lengthen rapidly.

lengthening than for slow shortening. This can be compared with that predicted by the original Huxley model (4.3 times) and a range of values from other experiments: ~ 1.0 (Aubert, 1956) to 6.0 times (Katz, 1939).

Fig. 2 shows a typical experimental record, the middle trace of which is force during the passive stretch. Only toward the end of each stretch was any measurable passive force generated. In some muscles pulled well beyond l_o, the passive force at the end of the stretch was substantial but no force-velocity data was taken from these experiments. The values for series elastic stiffness (K_{SE}) compare favorably with those that can be derived from Fig. 8 of Jewell and Wilkie (1958) for frog sartorius
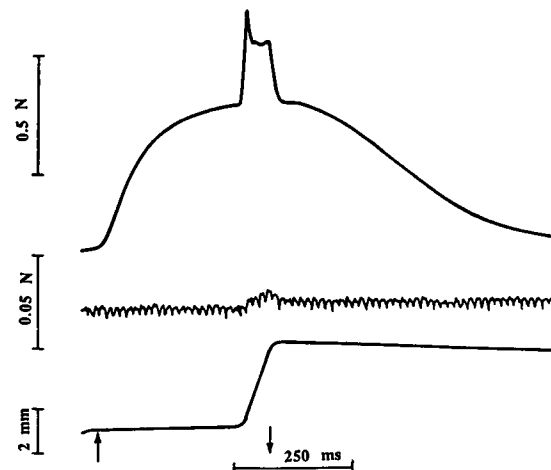

FIGURE 2 Experimental tracings from an isovelocity stretch of active muscle. The active force (top), passive force (middle), and length change (bottom) are shown as functions of time. Up and down arrows indicate when stimulation started and stopped, respectively. Noise in the force transduction (apparent in the magnified passive force trace) never exceeded 0.01 N peak-to-peak. Ramp velocity was 60 mm/s.

muscle. One problem with correcting for the series elasticity in this manner is that the stiffness was measured at forces below isometric but was applied to the data when the force was well above isometric. Whereas there is no reason to assume that K_{SE} is linear over this range of force, we presume that the measured stiffness was less than that appropriate for the force level at which the correction was made, that is K_{SE} is stiffer at higher force. Hence, the estimate of the portion of end-to-end velocity taken up by the series elasticity is an upper bound to that which did occur.

Quite apart from the force-velocity measurements, a surprising but reproducible phenomenon was observed in muscles that were stretched to lengths well beyond l_o. Fig. 3 shows muscle force as a function of length during two stretches of the same muscle at -0.3 V_{max}. One stretch began at l_o while the other began at $l_o + 4$ mm; both ended at $l_o + 6$ mm, some 20% longer than the rest length. The dashed curves are force records that include the contributions of passive components; the continuous curves show developed tension (passive contribution subtracted). In both cases force continues to rise throughout the stretch despite the fact that isometric capability of the muscle, as measured with twitches, drops over this range of muscle lengths. At $l_o + 6$ mm, for example, the isometric force dropped to 75% its peak value at l_o.

Computer simulations

Results of force-velocity simulations based on the three different linear cross-bridge models are shown along with
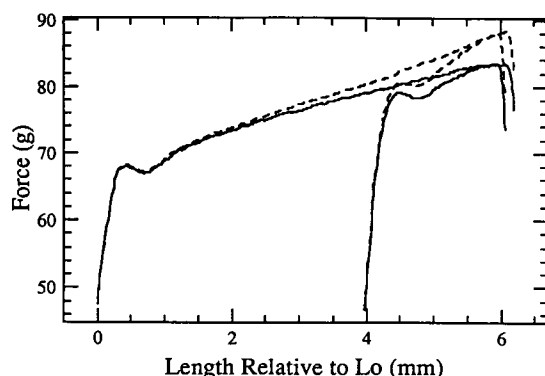
FIGURE 3 Force rises during stretches beyond l_o. Velocity of stretch was -0.3 V_{max}. Dashed curves are force including the passive contribution. Solid curves show developed force computed by subtracting a record of force from a subsequent passive stretch of the muscle at the same velocity. During isovelocity stretches to lengths well beyond l_o, force was seen to continue to rise or remain level. This is contrary to the expectation based upon the tension-length relationship of muscle. At long lengths, there should be reduced myofilament overlap and force should fall with increasing length.

the experimental data in Figs. 4, a–d (solid curves). Because the models differ only in predictions of the behavior during lengthening, each predicts the same force-velocity curve for shortening. Although not readily apparent in the graphs, the slope discontinuity at $V/V_{max} = 0$ is also the same for each of the models. This is because the constants f_1, g_1, and g_2, which are the same in all the models, determine the force-velocity behavior for slow lengthening. However, the model predictions diverge rapidly at higher lengthening velocity.

The force-velocity relationship calculated from the original Huxley model is shown with the experimental results in Fig. 4 A. The model clearly overestimates force for stretches, the asymptote at very high velocities being 5.33 P_o. Fig. 4 B compares simulations for a range of values for the Zahalak parameter g_3. Higher values for g_3 indicate a higher detachment rate for cross-bridges stretched beyond h. The dashed curve labeled H is the original Huxley 1957 model, i.e. $g_3 = 0$ s^{-1}. The other curves in the figure show simulations with $g_3 = 20, 40,$ and 60 s^{-1}, the overall effects being to introduce a local force maximum in the range $-0.4 \leq V/V_{max} \leq -0.2$ and a lowered force asymptote at high velocities. When $g_3 = 60$ s^{-1}, the predicted force-velocity relationship agrees best with the experimental results, although the predicted force does drop below the measured force at large velocities of lengthening.

Using $g_3 = 60$ s^{-1}, simulations in which a maximum allowable cross-bridge strain was also imposed are shown in Fig. 4 C. The predicted force is seen to fall as velocity increases; the high speed asymptote is zero in every case. As the maximum allowable strain is reduced (G approaching 1), the force falls more rapidly to zero and clearly departs from the experimental result. Even allowing cross-bridges to remain attached to lengths as long as 5h still noticeably reduces the force predicted in high-speed lengthening. The implication is that cross-bridges remain attached to lengths beyond 5h and continue to contribute substantial force during high-speed stretches.

This rather surprising statement may appear to result simply from a judicious choice of parameters g_3 and G. It may be presumed, for example, that by reducing g_3 to 40 the data may be fit with similar accuracy by using a G of 3. This is not the case (Fig. 4 D). When g_3 is made <60 s^{-1}, the model predicts forces during slow stretches well above those found experimentally, a result that cannot be improved by imposing a low maximum strain. We found, in fact, that the correspondence between experimental and predicted results is notably diminished when g_3 was made <50 s^{-1} or $G < 5$, regardless of the combination of the two.

Finally, in Fig. 5, A and B, simulations based on the nonlinear cross-bridge model are shown (dashed curves are results using linear cross-bridges). Because we
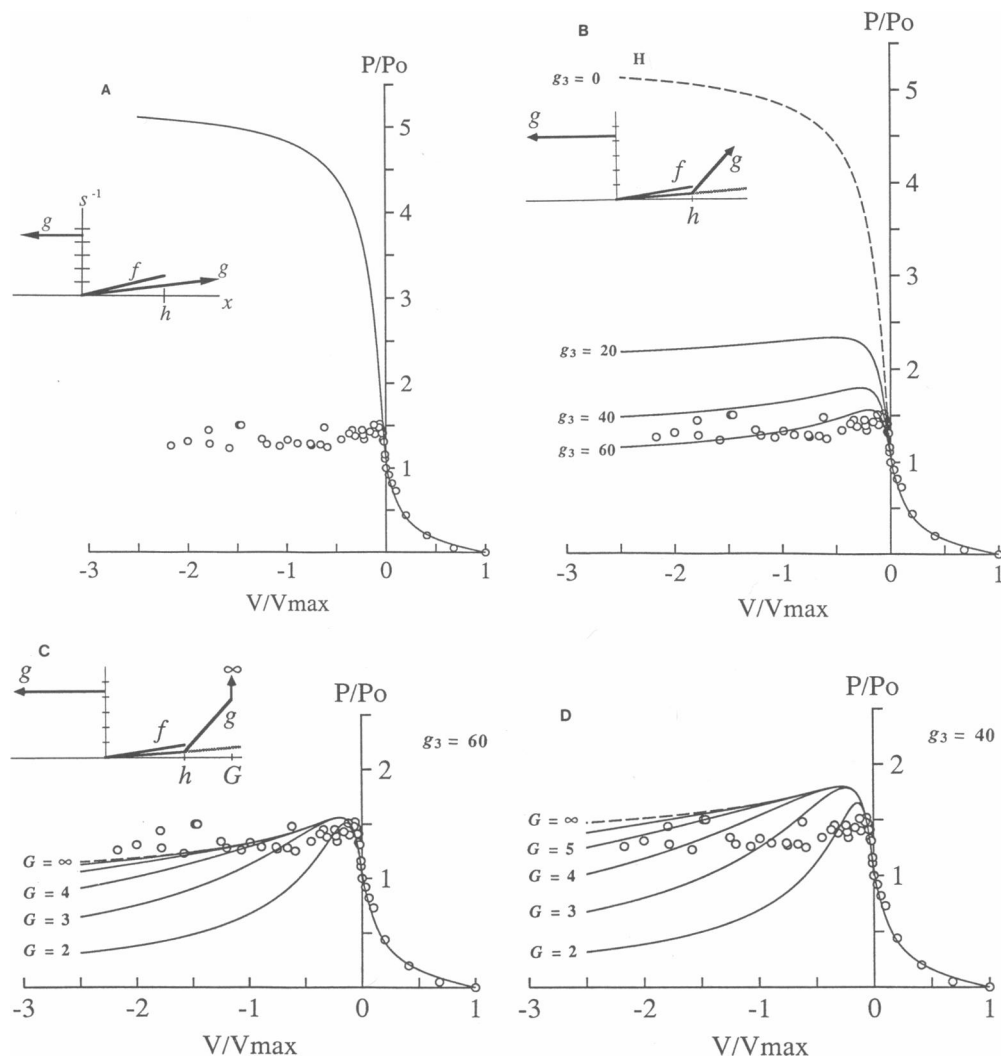
FIGURE 4 Comparisons with theoretical predictions. (*A*) The force-velocity relationship as predicted by the original Huxley (1957) cross-bridge cycling model (*solid curve*) matches the experimental data (*circles* replotted from Fig. 1) only for velocities $V \geq -0.1\ V_{max}$. In this model, the force asymptote for high-speed stretches is 5.33 P_o. The form of the attachment/detachment rate functions as specified by Huxley are shown (*inset*). (*B*) Increasing the slope of the detachment rate function beyond $x = h$ (Zahalak, 1981; *inset*) decreases the predicted asymptotic force and introduces a local force maximum in the range $-0.4\ V_{max} \leq V \leq -0.2\ V_{max}$, features which are mirrored in the experimental data. Force-velocity curves computed using three values for g_3, 20, 40, 60 s^{-1}—(*solid curves*), are compared to the Huxley prediction (*dashed curve*). When $g_3 = 60$ s^{-1}, there is close correspondence with the experimental data. (*C*) A maximum strain condition requires cross-bridges to detach when stretched beyond a specified length (Ward, 1987; *inset*). When the maximum strain condition is incorporated into the Zahalak model with $g_3 = 60$ s^{-1}, predicted force falls below the experimental values (*solid curves*). The difference between the curves $G = 5$ and $G = \infty$ (*dashed curve*) implies that cross-bridges remain attached beyond $5h$ when muscle is forced to lengthen rapidly. (*D*) Other combinations of g_3 and G do not yield equivalent results. This is the case $g_3 = 40$ s^{-1} with a range of values of G.

restricted our attention to nonlinearities that increase stiffness with cross-bridge length, it was sensible to add the nonlinearity only to those models that underestimated force at high stretch velocities. From Fig. 4 *C*, it is clear that when $g_3 = 60$ s^{-1} and $G = 2$, the linear cross-bridge model grossly underestimates force at at high velocities of stretch. Adding cross-bridge nonlinearity can raise the predicted force at high stretch velocities nearer to the experimental values. With cross-bridge force described by

$$P_{cross\text{-}bridge} = k(x + 0.1e^{2.4x}),$$

the force of a cross-bridge stretched to its maximum, i.e., $2h$, is approximately seven times that of a linear cross-bridge stretched the same amount. As may be expected,
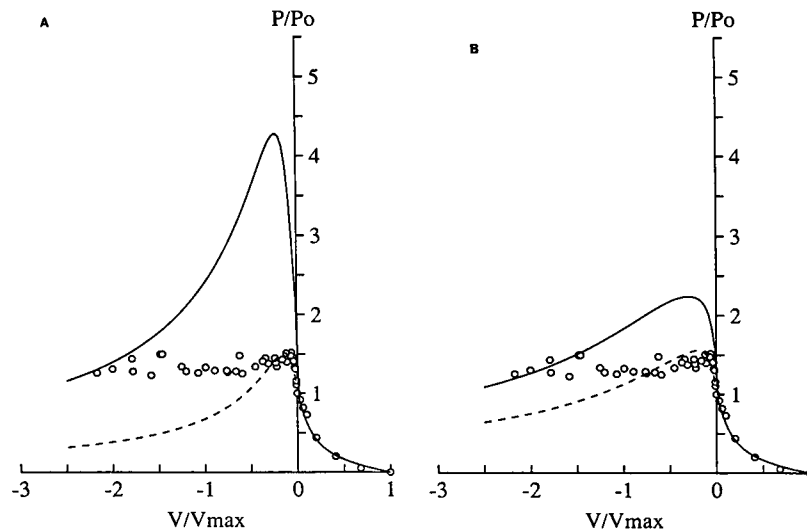
FIGURE 5 Effect of nonlinear cross-bridge stiffness. This was investigated as a way to improve the fit of the maximum cross-bridge strain model. A large nonlinearity can, in fact, bring the predicted force at high velocities up to the level observed in experiment, but there is a concomitant overestimation of force for slow lengthening. Solid curves are nonlinear results; dashed curves show linear results from previous figures. (A) Maximum allowable strain was set to $2h$ and a nonlinearity of the form $P_{cross-bridge} = k(x + 0.1e^{2.4x})$ was introduced. (B) When maximum strain was increased to $3h$, a less severe nonlinearity, $P_{cross-bridge} = k(x + 0.1e^{1.25x})$ was required to bring the force above isometric, but the high force during slow lengthening persists.

by increasing the force at high speeds by adding such a nonlinearity, a substantial overestimate of force occurs at low stretch velocities. Allowing cross-bridges to remain attached to $3h$ (Fig. 5 B) permits a less severe nonlinearity to be employed to match the high-velocity results,

$$P_{cross-bridge} = k(x + 0.1e^{1.25x}),$$

but the overestimate of force at low velocity persists.

DISCUSSION

Experiments

The experimental results extend previous knowledge of how muscle performs when forced to lengthen while active. Our force-velocity data are similar to those reported by Flitney and Hirst (1978) for stretch speeds up to 1 V_{max}; we know of no published data with which to compare our results in faster stretches. In a general sense, our data demonstrate how very robust active muscle is when subjected even to severe stretches. Each data point in Fig. 1 represents an average from two identical isovelocity stretches on the same muscle, meaning that there was never enough irreversible damage to make completion of the mirror-pairs protocol impossible. This is true despite the fact that, in the fastest stretches, the muscles were absorbing more than 30 times the maximum power

(force times velocity) that can be produced by shortening muscle.

The phenomenon of force continuing to rise when the muscle is stretched beyond its rest length is apparent in many published experimental records (e.g., Joyce, 1969; Edman, 1978). However, no one has discussed it at any length or sought to explain it. No existing single-sarcomere cross-bridge model can account for this phenomenon of force rising beyond l_0. Typically, cross-bridge models assume that the muscle is always on the plateau of its tension-length curve, i.e., that there are no sarcomere length effects of the sort described by Gordon et al. (1966). In fact, if a tension-length relationship were added, it would serve only to reduce the predicted force of the model as it is stretched beyond l_0. Hence, the modeling described below pertains only to the force-velocity results. (See the following paper for a description of a multisarcomere model that succeeds in reproducing the rising force beyond l_0.)

Modeling

The 1957 cycling theory remains the most effective means for explaining how cross-bridge dynamics result in the shortening force-velocity curve. But can the same theory, even with modifications to improve its correspondence to experimental results, explain the lengthening force-velocity curve? Apparently not. The line of reasoning is this: if

a single-sarcomere, mathematical model is proposed to behave as a real muscle under conditions of high-velocity stretch, the mechanical properties that must be presumed for cross-bridges in the model are beyond "reasonable." It is, of course, impossible to know without doubt what the characteristics of cross-bridges are, but a result from the model that requires cross-bridges to remain attached at such long lengths calls into question the basic, single-sarcomere premise.

It is, by now, an established fact that intersarcomere dynamics play a role in many muscle phenomena. The failure of the single-sarcomere model to predict the lengthening force-velocity curve suggests that sarcomere inhomogeneities may be, in this case too, a predominant factor. In effect, this puts an additional severe limit on the applicability of cross-bridge cycling theories in explaining macroscopically observable behaviors of muscle. The implication is that, even as it applies to the most fundamental mechanical aspects of muscle, reliance upon a single-sarcomere model may be inadequate.

APPENDIX

This appendix provides the analytical expressions used to compute the force-velocity curves in the various models. The equation for shortening, which is in common for all the models, is included for completeness.

Constants in the Huxley (1957) model

The attachment, $f(x)$, and detachment, $g(x)$, rate functions are given as

$$
\begin{array}{lll}
x < 0 & : \quad f(x) = 0; & g(x) = g_2; \\
0 \le x \le h & : \quad f(x) = f_1 x/h; & g(x) = g_1 x/h; \\
x > h & : \quad f(x) = 0; & g(x) = g_1 x/h;
\end{array}
$$

where $f_1/h = 43.3 \text{ s}^{-1}$, $g_1/h = 10.0 \text{ s}^{-1}$, $g_2 = 209.0 \text{ s}^{-1}$. Under isometric conditions, cross-bridges are found only in the range $0 \le x \le h$. In the expressions that follow, P is force normalized by the isometric tension P_0 and v is velocity of shortening normalized by V_{max}.

Steady shortening

$$
P(v) = 1 - \frac{2(v/h)}{f_1 + g_1} \left\{ 1 - \exp\left[-\frac{(f_1 + g_1)}{2(|v|/h)} \right] \right\}
$$
$$
\cdot \left(1 + \frac{f_1 + g_1}{g_2} \cdot \frac{(v/h)}{g_2} \right).
$$

Huxley 1957 model: steady lengthening

$$
P(v) = 1 + \frac{2(|v|/h)}{f_1 + g_1} \cdot \frac{f_1}{g_1} \qquad \cdot \left\{ 1 - \exp\left[-\frac{(f_1 + g_1)}{2(|v|/h)} \right] \right\}
$$

$$
P(-\infty) = \frac{f_1 + g_1}{g_1}.
$$

Zahalak 1981 model: steady lengthening

The change suggested by Zahalak was an increased slope in the detachment rate function beyond $x = h$:

$$
g(x) = g_1 x/h + g_3(x/h - 1) \quad (x > h).
$$

The closed-form expression (Ward, 1987) for steady lengthening in this model is

$$
P(v) = 1 + \left\{ 1 - \exp\left[\frac{-(f_1 + g_1)}{2(|v|/h)} \right] \right\} \left(-\frac{2(|v|/h)}{f_1 + g_1} + \frac{2(|v|/h)}{g_1 + g_3} \right.
$$
$$
+ \frac{g_3}{g_1 + g_3} \left[\frac{2\pi(|v|/h)}{g_1 + g_3} \right]^{1/2} \exp\left[\frac{g_1^2}{2(|v|/h)(g_1 + g_3)} \right]
$$
$$
\left. \cdot erfc\left\{ \frac{g_1}{[2(|v|/h)(g_1 + g_3)]^{1/2}} \right\} \right)
$$

$$
\lim_{v \to \infty} P(v) = \frac{f_1 + g_1}{g_1 + g_3} + [\text{terms of order } |v|^{-1/2}],
$$

where $erfc()$ is the "complementary error function" defined as

$$
erfc(x) = \frac{2}{(\pi)^{1/2}} \int_x^\infty e^{-t^2} \, dt.
$$

Both the asymptotic and general expressions reduce to the Huxley result if $g_3 = 0$. The force at high stretch velocities is still nonzero but is reduced in magnitude by the added g_3 term in the denominator.

Maximum cross-bridge strain model (Ward, 1987): steady lengthening

$$
P(v) = 1 + \frac{2(|v|/h)}{f_1 + g_1} \cdot \left\{ 1 - \exp\left[\frac{-(f_1 + g_1)}{2(|v|/h)} \right] \right\}
$$
$$
\times \frac{f_1}{g_1} \left\{ 1 + \frac{f_1 - g_1}{g_1} \exp\left[\frac{-g_1(G^2 - 1)}{2(|v|/h)} \right] \right\}
$$

$$
\lim_{v \to \infty} P(v) = \frac{f_1 + g_1}{2(|v|/h)} (G^2 - 1) + (\text{terms of order } |v|^{-2}).
$$

The Huxley force-velocity expression for lengthening can be recovered by letting $G \to \infty$. A closed-form expression has not been derived for the case when the maximum strain condition is added to the Zahalak model. The theoretical curves in Fig. 4, C and D, were computed numerically.

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