

Discrete values of displacement rate and
developed force in sliding filaments

by

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During the later years increasing evidence has turned out in favour of the sliding filament mechanism of muscle motility.^{1,2,3} According to this model the myosin cross-bridges in the overlap region of the actin and myosin filaments undergo cyclic configurational changes. During a part of the cycle the cross-bridges are attached to active sites on the actin filament, and relative motion between the two filaments results from the configurational changes during this part of the cycle. In the rest of the cycle the cross-bridges are unattached while undergoing recovery in preparation for the next cycle. Splitting of ATP probably takes place only when the myosin is attached to the actin². While the time spent in the active phase might then be related to the rate of ATP splitting, the time spent in the recovery phase more likely depends on characteristics of the myosin, in which case the recovery time is independent of sliding rate. It has been suggested^{2,3} that the configurational changes taking place during ATP splitting are specific for the molecule complex involved, and therefore that "the cross-bridges are likely always to need to go through exactly the same structural cycle during the splitting of

ATP and the performance of mechanical work" ². If this is so all cross-bridges should undergo the same changes, and filament displacement during the active phase should be a constant of the system. It has been pointed out ² that the cross-bridges must move asynchronously for a steady force to be developed along the filaments. The equal cross-bridges can only move in this way if their repeat distance is different from the repeat distance of the attachments points. This difference is a well known feature of the myofibril ⁴.

Consider a sliding filament system where the time t_b spent in each recovery is constant and independent of the rate of sliding. This rate of sliding v can be expressed by the filament displacement d during the active phase and the time t_a spent in this phase

$$v = \frac{d}{t_a} .$$

The set of cross-bridges and the set of active sites are nearly in phase - respectively out of phase - like the line sets of a Moiré pattern, in the same way as two interfering waves of different wavelengths form beats. If the repeat distance d_b of the cross-bridge set is larger than the repeat distance d_a of the active site set - the analysis is equivalent in the opposite case - the distance l between neighbouring phase repeats is given by

$$\frac{1}{l} = \frac{1}{d_a} - \frac{1}{d_b} ,$$

or

$$l = \frac{d_a d_b}{d_b - d_a} .$$

The number p of cross-bridges in the length l is then

$$p = \frac{d_a}{d_b - d_a}, \quad (1)$$

since $l = pd_b$. When the cycle of configurational changes is the same for all cross-bridges the cross-bridge must be at a proper distance and orientation from the active site for attachment to take place. This implies that attachment can only occur at a proper phase of the interference pattern, and thus that there must be an integer number n of pattern repeats between each region of attachment. The distance s between such regions is thus a multiplum of the repeat distance l ,

$$s = nl.$$

Since there are p cross-bridges in l there are np cross-bridges in s , of which a are active and $b = np - a$ are recovering. Geometrical considerations show that the number of attached cross-bridges in each region of attachment is defined by

$$a = \frac{d}{d_b - d_a}, \quad (2)$$

and thus a is constant.

The ratio between the number of active cross-bridges and the number of recovering cross-bridges must be equal to the ratio between the times spent in the active and the recovery phases

$$\frac{a}{b} = \frac{t_a}{t_b}. \quad (3)$$

A change in the sliding velocity is effectuated by a change in t_a , and (3) shows that with constant t_b this also causes a

change in the ratio a/b and thereby in the geometry - the "gait" - of the motion. But a is constant and $b = np - a$, and the ratio cannot be changed randomly. Thus by (3)

$$v = \frac{d}{t_a} = \frac{d}{t_b} \frac{b}{a} = \frac{d}{t_b} \frac{np-a}{a}$$

or, by (1) and (2),

$$v = \frac{d}{t_b} (nd_a - d) . \quad (4)$$

In addition to parameters of the sliding filament mechanism this expression for the sliding rate contains only the number n of pattern repeats between each region of cross-bridge attachment. Sliding can only occur at the rates defined by the integer values of n , and there is therefore a discrete set of allowed sliding rates between the two filaments.

If the average force in each active cross-bridge is f the force developed in each region of attachment is af , and the force developed in the pattern repeat length - a parameter of the system - is

$$F = \frac{1}{n} af = \frac{1}{n} \frac{fd}{d_b - d_a} \quad (5)$$

where n is again the integer number of pattern repeats between regions of attachment. Thus to each allowed value of the sliding rate there corresponds a distinct value of the developed force.

Due to the polarity of the system, active sliding of the myosin and actin filaments is always in the direction corresponding to muscle contraction^{5,6}. If the myofibril is allowed to contract from a state of no sliding and all cross-bridges attached, the rate of contraction must be according to (4), while the corre-

sponding number of cross-bridges that must be released is $b = np - a$. Our analysis does not tell how the sliding filament mechanism behaves under forced stretching of an active myofibril, however.

Experiments on muscles must be performed on sections containing a vast number of myofibrils, and muscle force and motion represent the integrated effect of these myofibrils. The "discreteness" of sliding velocity and developed force in each myofibril is then not easily detected in the muscle's dynamics. (4) and (5) may, however, be combined to give

$$F(v_s + \frac{d}{t_b}) = f \frac{d_a}{d_b - d_a} \frac{d}{t_b} ,$$

or more roughly

$$F(v_s + \text{constant}) = \text{constant} ,$$

which may be compared with Hill's experimentally determined relation

$$(F + \text{constant})(v + \text{constant}) = \text{constant}$$

for the whole muscle.

The sliding filament mechanism has also been suggested as the source of motion in cilia and flagella ^{8,9,10,11}, where sliding supposedly occurs along the nine peripheral filaments found in these organelles ¹². It has been found ^{9,13} that when a plane bend propagates along the organelle the radius of curvature of the bend remains nearly constant. It is easily found that in such bends the rate of sliding between a peripheral filament and the surrounding matrix is

$$v = (c/R)\Delta R , \tag{6}$$

while the rate of sliding between neighbour filaments denoted by i and $i+1$ is

$$v = (c/R)(\Delta R_{i+1} - \Delta R_i) . \quad (6')$$

Here c is the rate of bend progression relative to the organelle, ΔR is the distance of the filament from the neutral plane of bending, and R is the radius of curvature of the neutral plane in the bend. In a plane bend ΔR is constant for each filament, and if active sliding takes place in the bends, it can only occur at the rates given by (4). When the progression velocity is constant, both (6) and (6') then show that only discrete values of the radius of bend curvature are allowed. That this result conforms with observations¹³ might be taken as evidence, both for the sliding filament mechanism as the source of ciliar and flagellar motility, and for the conclusions of the present analysis.

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