LETTER TO THE EDITOR

Reply to Diamond et al. by A. Babu and J. Gulati

Dear Sir:

Original experimental observations and their interpretations are two separate considerations, but this distinction is not firmly observed in the preceding letter by Diamond et al. (1986). Thus, contrary to their opening statements, skinned fibers from the frog exhibited a slight increase in Ca^{2+}-activated force under low level lateral compressions by dextran T500 in our experiments (Gulati and Babu, 1985), and accordingly there is now at least qualitative agreement among the experimental findings in the various reports cited in the preceding letter.[1]

The main point of difference between the different studies is in the interpretation. By using correction factors linked to the possible reductions in ionic strength in relation to the amount of added dextran, we found that force of the fiber and hence, force per bridge, was constant over a wide range of fiber compression, supporting the assumption of Gordon et al. (1966) to explain the length–tension relationship for sarcomere lengths $\geqq 2.2\ \mu m$. Diamond et al. note that our corrections are not linked simply to mole fractions that are changed by the additions of dextran because the partial molality of each electrolyte is held. A corresponding decrease in activity coefficients (due to a change in the standard state) in the presence of dextran is still a possibility. Another possibility of sequestration of the ionic species was, however, questioned by them on the basis of unpublished Donnan calculations.

Comparisons of pCa–force relationships with new data under different conditions is made by Diamond et al. in efforts to reject any possibility of ionic changes in dextran solutions, but their results are inconclusive. The initial observation that Ca^{2+}-sensitivity was enhanced at low levels of dextran concentration was consistent with the idea that effective ionic strength may be reduced. The interpretation was complicated, however, because the effect on Ca^{2+}-sensitivity was reversed when more dextran was added.

We suggest, therefore, that the final conclusion of Diamond et al. challenging the standard interpretation for the descending part of the length–tension relationship on frog fibers (i.e., force levels are characterized by actin–myosin overlap) requiring constant force per bridge on compression is provocative but unconvincing. Our earlier results on compression of intact fibers also suggested that force per bridge was constant with compression (Gulati and Babu, 1982, 1984). The results of osmotic changes (with sucrose and KCl) on intact fibers were perhaps more straightforward for resolving the present issue for cross-bridge mechanism, because in that protocol no increase in force was seen at low level compressions. These studies rule out any major effects on force per bridge.

On the basis of the conclusion of relative insensitivity of isometric force by the cross-bridge on the compression of the lattice over a significant range, we had suggested that cross-bridges may undergo very little movement in the head region. This is consistent with a number of other studies (Cooke et al., 1982; Fajer et al., 1985). In addition, the somewhat less controversial precipitous drop in force of skinned fibers at much higher compressions (beyond the range studied with intact fibers) suggested to us that nevertheless some flexibility within the cross-bridge head was critical for contraction. This idea is now under further study (Tregear, 1986).

Received for publication 5 August 1986.

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[1] One exception is in the report by Maughan and Godt (1981) where force of frog fibers fell at moderate compressions. Explanation for this discrepancy is not clear, although some possibilities have been mentioned (Gulati and Babu, 1982, 1985).