**Jülicher and Prost Reply:** In Ref. [1], we demonstrate the possible existence of dynamic transitions in the steady states of many coupled molecular motors moving along a linear filament. The prediction is that the transitions "should be observable in motility assay experiments with a high concentration of motor molecules." In order to experimentally test this prediction, simple systems are necessary which consist of only purified motors and filaments. Recently, the first force-velocity curve of the purified actin-myosin system at high motor density has been obtained in a motility assay [2]. One result is the observation of the signature of a dynamic first-order transition of the type predicted by our work [see Fig. 1(a)].

What are the consequences for muscles? Muscles are complex biological systems which contain contractile elements, called sarcomeres [see Fig. 1(b)]. Within each sarcomer, myosin filaments $(m)$ slide with respect to actin filaments $(a)$. The myosin filaments are connected via elastic elements such as titin molecules $(t)$, which we represent for simplicity by Hookian springs, to the $Z$ disks separating sarcomeres $(z)$ [3]. This sarcomere structure does not allow for steady states with nonzero velocity; muscle contraction is always transient behavior. As a consequence, the dynamic transition of the purified system is replaced by filament oscillations via a Hopf bifurcation [4]. This leads to the prediction that muscles can have oscillating regimes within parameter space. Spontaneous oscillations are indeed observed in ordinary skeletal muscles [5,6]. The characteristic behavior observed for muscle myofibrils matches closely the oscillations obtained from our model. Oscillation frequencies in our model depend on the elastic modulus of the spring and can vary between zero and a maximal value, a range fully consistent with observed frequencies [4]. Recently, it was demonstrated that these oscillations are due to the properties of the force-generation mechanism alone: They continue to exist if troponin-tropomyosin, which are regulatory enzymes, are removed. The authors of this paper concluded that a natural explanation of this observation is an instability of the force-generating mechanism as described by our model [6].

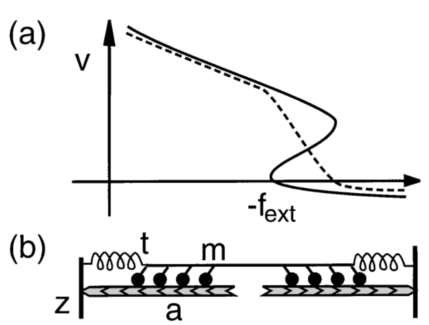


FIG. 1. (a) Velocity $v$ of steady states as a function of force $f_{\mathrm{ext}}$ for a first-order transition (solid line). Averaged behavior over the stable branches (dashed line). (b) Schematic arrangement of filaments in muscle sarcomeres.

The Comment of Marin *et al.* [7] is deeply flawed and based on a misunderstanding of our predictions, as we explain in four points: (i) For muscles, we do not predict dynamic transitions between steady states. The signature of unstable behavior is oscillations which have been observed [5,6,8]. (ii) Marin *et al.* compare naively a curve $v(f_{\mathrm{ext}})$ for single filaments in steady state with the behavior observed for muscles. As explained, the two should not be compared directly; muscle experiments probe the transient response of many individual filaments. The resulting averaged behavior shows no transition [see Fig. 1(a)]. There is, however, evidence for unstable behavior in the same experiments: the author of Ref. [8] reports in the discussion the observation of oscillations as an unwanted effect that was reduced using feedback systems. (iii) Even if a comparison of single filament behavior and muscle data was licit, the way it is done by Marin *et al.* does not make any sense. A critical point, which is of measure zero and can only be reached by a fine-tuning of parameters, is compared to experimental data where no parameter has been specifically adjusted. Furthermore, only a short segment of the experimental data is displayed. This segment contains the large-force regime that probably corresponds to a different physics such as forced rupture of cross bridges. (iv) The main point of the Comment, namely, the "fact" that "instabilities or unstable motion have not yet been observed experimentally in muscle," is contradicted by Refs. [5,6,8].

In summary, there is strong experimental evidence that the instabilities predicted by Refs. [1] and [4] do exist.

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