# Comments to the Editor

## Response to "On Phosphate Release in Actin Filaments"

Jégou et al. disagree with some of the findings of our article (1). They argue that 1), a different value of the release rate $r_d$ can improve the fit to depolymerization dynamics obtained by the random release model; 2), plotting depolymerization dynamics of single filaments would be more appropriate than comparing an average to a single filament; and 3), data in their article (2) for the dependence of the phosphate time courses on initial actin concentration (during growth) supports the random release model. We have the following responses to these arguments:

1. Jégou et al. appear to have misunderstood our arguments regarding the different values of $r_d$. They interpret our argument as saying that for $r_d = 0.0074\ s^{-1}$, "the resulting curves do not agree well with the data." On the contrary, we felt that the agreement for this $r_d$ is quite close, and we explicitly stated that "they fit the depolymerization data well." Our argument is that no random model using the same value of $r_d$ can fit both the data of Jégou et al. (2) and the data of Melki et al. (3). The inability of the random model to fit multiple datasets with a single value of $r_d$ provides motivation for considering correlated release models. Jégou et al. also mention the difference between the $0.0045\ s^{-1}$ rate they used to fit a particular filament trace versus the average value of $0.0074\ s^{-1}$ that we used. We feel that it is preferable to work with the average value of $0.0074\ s^{-1}$ rather than the single-filament value, because the value of $r_d$ should not vary from filament to filament.
2. We hesitate to base validation of our model on comparison of a calculated single-filament depolymerization trace from the simulations to the experimental curve from a single filament. To do this, one has to choose a single run from many runs, and this will lead to cherry-picking where one run can almost always be found that matches the experimental data. The most rigorous comparison would be to measure depolymerization statistics of many filaments, evaluate quantitative measures from these such as velocity distributions and time correlation functions, and compare these to the corresponding theoretical predictions. When looking at a single filament, it is certainly true that the average time course misses information. Thus, we felt that the best approach was to supplement the average time course with a number of individual filament time courses, as we did in Fig. 6 of Burnett and Carlsson (1). To avoid bias, we simply presented the first 10 filament traces from the simulations. Subsequent simulation runs showed fewer fluctuations than the first 10, and their fluctuations are comparable to those of the experimental data.
3. To obtain quantitative bounds on the cooperativity, we can work only with the data that are presented in Jégou et al. (2). The inset to Fig. 4 *E* of that article presents data for the depolymerization velocity as a function of time at a lower actin concentration. In this inset, and in the main figure, transitions are seen from slower to more rapid depolymerization. The rates extracted from these transitions differ by ~40%. It is not clear what bounds the difference places on the cooperativity. Our analysis was based directly on single-filament depolymerization time courses, but an analysis of the data presented in Fig. 4 *E*, using a stochastic treatment of polymerization, would be informative.

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## REFERENCES

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