Supporting Information

Dystrophin As A Molecular Shock Absorber

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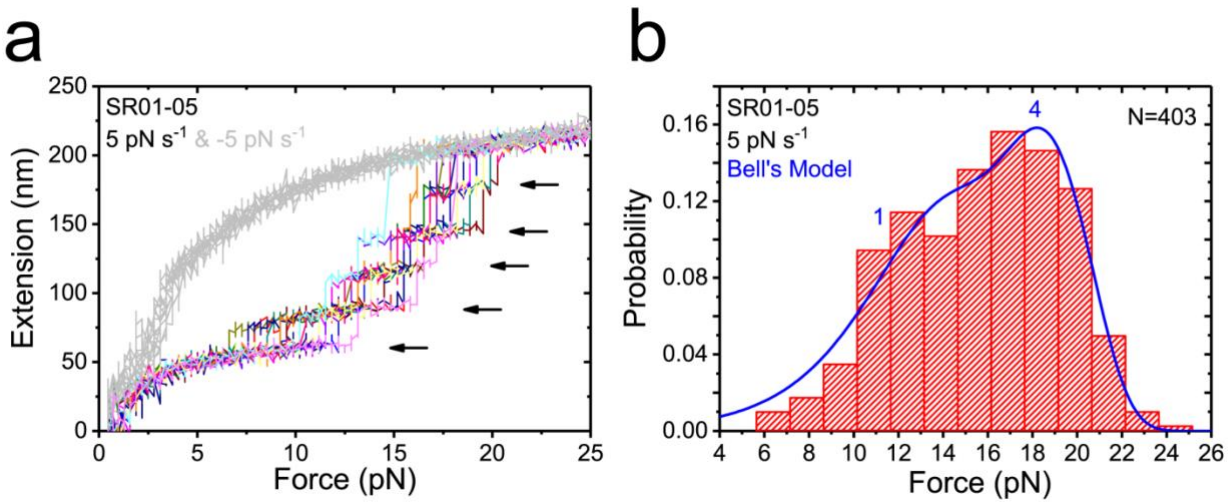
*Supporting Text S1--Kinetic simulation based on revised Gillespie algorithm***.** The kinetic simulation used in the study is based on a revised Gillespie algorithm for faster calculation. The Gillespie algorithm stochastically determines the time of the next transition (τ) from the current state, and stochastically chooses one of the available transitions, based on the current unfolding and refolding rates that are dependent on the current tension in the molecule. However, in our simulation, the molecule is stretched by certain pulling rates. If the stochastically determined time of the next transition is too long, the tension in the molecule could increase significantly during the time before the next transition takes place. To prevent this, we imposed a constraint that during the time before the next transition occurs, the extension change must be smaller than 0.1 nm. When the stochastically determined value of τ does not satisfy this constraint, we advance the simulation by a small time step Δt, recalculate the force based on the updated extension, and recalculate the probabilities of each of the available transitions based on the corresponding force-dependent rates.

In the Gillespie algorithm, we choose between the possibilities of available transitions in such a way that the probabilities $P_{u,f}^{i}$ are directly proportional to the rates $k_{u,f}^{i}(F)$, where $i = 1, \ldots 24$ denotes the position of the SRs, and u, f denotes the unfolding/refolding of the domain. A random number is generated to decide on which transition will proceed. A second random number homogeneously distributed over [0, 1] is generated to determine the value of τ. The exact formula is $\tau = -\frac{\ln Rand()}{\sum_i k_{u,f}^{i}(F)}$.

Supporting Text S2-- Bootstrap analysis. To obtain the mean, standard error of the kinetic parameters of unfolding/refolding transitions, we employed the bootstrap analysis to the experimental data of the unfolding/refolding forces for each dystrophin segment. Briefly, in single-molecule stretching experiments, a data set with a size of *N* number of data points of the transition forces is obtained experimentally. We generate another 4 sets of data points, each with a size of *N*, by randomly data-picking from the original experimental data set. Thereby, there will be 5 sets of data points, each with a size of *N*. Then, we fit each set of data by the models mentioned in the main text, and obtain 5 sets of the kinetic parameters. The mean value and standard error of the kinetic parameters are therefore obtained from the 5 sets of the kinetic parameters.

Supporting Figure



Supporting Figure S1. The unfolding dynamics of the dystrophin SR01-05 with a loading rate of 5 pN s^{-1}. (a) the force-extension curves of the unfolding transitions of the dystrophin SR01-05 at 5 pN s^{-1} (colored). The black arrows indicate the positions of unfolding events. The grey curves are the refolding of the SR01-05 at a loading rate of -5 pN s^{-1}. (b) The resulting normalized histogram of the unfolding forces of SR01-05 with a loading rate of 5 pN s^{-1}. The blue line is the Bell's Model curve with parameters obtained from SR01-05 with a loading rate of 1 pN s^{-1}, described in the main text. N=403 data points were obtained from multiple (>5) independent experiments.