

Simulation model for combined motion of myosin cross-bridges agrees with experimental data

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1. ABSTRACT

The motivation for this work was to derive a theoretical model for the combined motion of a sample of muscle tissue with a small number (approximately 12) of myosin molecules. This was then compared to data collected at the University of North Texas Health Science center. A theoretical model of the motion of the myosin cross-bridges has been derived. The solution is a combination of solutions from the classical harmonic oscillator, Brownian motion, and Maxwell-Boltzmann statistics. The model illustrates the myosin behavior as a function of the number of myosin molecules, the temperature of the sample, and the spring constant. The results show that there is good agreement between the theoretical model and experimental data.

2. INTRODUCTION

The motivation for this work was to derive a theoretical model for the combined motion of a sample of muscle tissue with a small number (approximately 12) of myosin molecules. This was then compared to data collected at the University of North Texas Health Science center. A theoretical model of the motion of the myosin has been derived. The solution is a combination of solutions from the classical harmonic oscillator, Brownian motion, and Maxwell-Boltzmann statistics. The model illustrates the myosin behavior as a function of the number of myosin molecules, the temperature of the sample, and the spring constant. The results show that there is good agreement between the theoretical model and experimental data

Simulation model of myosin with experimental data

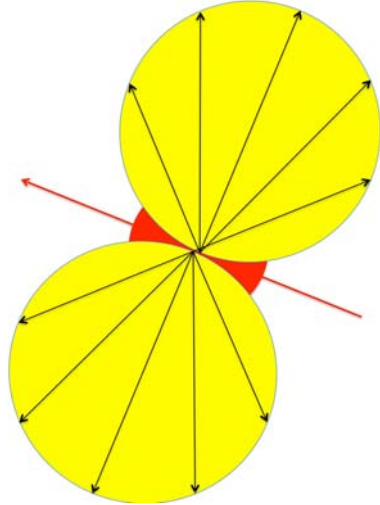


Figure 1. Dipole radiation from fluorescent molecule.

3. THEORETICAL MODEL

The preparation of myofibrils, expression of LC1 and labeling is elaborated in the first referenced paper¹ in the reference section. Here we will focus on the basic physics of the measurement of the position of the myosin. In Figure 1 we see the fluorescent molecule and the dipole radiation pattern emitted once excited. In Figure 2 we see that the fluorescent molecule has been attached to the myosin cross-bridge of the myosin and radiates when excited by a laser¹. As the myosin oscillates back and forth it is clear that the intensity of the radiation changes, depending on the angle of the fluorescent molecule and the associated parallel and perpendicular components will vary. The light emitted is collected by the apparatus, split into two beams, and then each beam passes through a polarizer filter each oriented to absorb one of the two components and allow the other to pass to the detector. This then allows each detector to measure the intensity of either the parallel or perpendicular component of the total field, from this information we may apply equation 1 to compute the average angular position (12,13,14,15,16). A PicoQuant MT 200 confocal system (PicoQuant, Berlin, Germany) coupled with an Olympus IX71 microscope had been used to acquire the fluorescence data.

Muscular contraction is achieved by sliding of thin actin filaments over the myosin heads with the chemical energy derived from ATP hydrolysis. In the various sub steps of the ATP hydrolysis induced myosin cross-bridge cycle, it is during the power stroke state that much of the angular displacement of the myosin head is attributed to. To study the motion and distribution of the orientations of myosin cross-bridges we used a sensitive fluorescence polarization based assay. The essential light chain 1 domain containing a single cysteine residue was labeled with a Setau maleimide or Rhodamine iodoacetamide dye (1). Therefore, each myosin has a fluorophore attached to the lever arm which fluoresces when excited by a laser¹. The light emitted is passed through a beam splitter and then passed through polarizers

that are oriented to allow light that is either horizontally or vertically polarized to pass to a detector (shown in Figure 2). The position is then calculated by the following equation

$$\phi = \frac{I_{\perp} - I_{\parallel}}{I_{\perp} + I_{\parallel}} \quad (1)$$

Where, I_{\parallel} is the intensity of the horizontally polarized light detected, I_{\perp} is the intensity of the vertically polarized light detected

Therefore, the measurement made is an average position of N number of myosin as shown in Figure 3. The total amount of light emitted by the fluorescent molecules is analyzed to give an average position of the myosin. Where, $x_1, x_2, x_3, x_N, x_{ave}$ are the positions of the first, second, third, and N th myosin in the sample and their average position, respectively.

The data, at first glance, seemed to have a sinusoidal behavior with a random *kick* yielding a random radial angle of position with an upper and lower limit. This was due to the fact that each myosin was at a different phase as it cycled through its motion, which yielded an average position that was random.

The derivation of the theoretical model began by using a sinusoidal motion to calculate the position, and velocity, which is represented by a linear classical harmonic oscillator illustrated in Figure 4 below.

Because the fluorescent molecule is attached to the lever arm of myosin, only the motion of the lever arm is being measured. For this reason a theoretical model employing simple harmonic motion is appropriate in comparison with experimental data.

The general solution for the harmonic oscillator model is given below. It is simply a sinusoidal motion, $\sin(\omega t)$ with an initial random position, x_{random} , calculated by Brownian motion and Maxwell-Boltzmann velocity distribution to calculate the *kick* in position, x_{ATP} . The derivation of the following model is given in section V below.

$$x(t) = A_0 \sin(\omega t) + x_{ATP} + x_{random} \quad (2)$$

The standard Gaussian distribution, or normal distribution, shown below for both the velocity and position, gives the probability distributions of finding the myosin at a velocity v or position x respectively.

$$P(v) = \frac{1}{\sigma_v \sqrt{2\pi}} e^{-\frac{1}{2\sigma_v^2} v^2} \quad (3)$$

$$P(x) = \frac{1}{\sigma_x \sqrt{2\pi}} e^{-\frac{1}{2\sigma_x^2} x^2} \quad (4)$$

Simulation model of myosin with experimental data

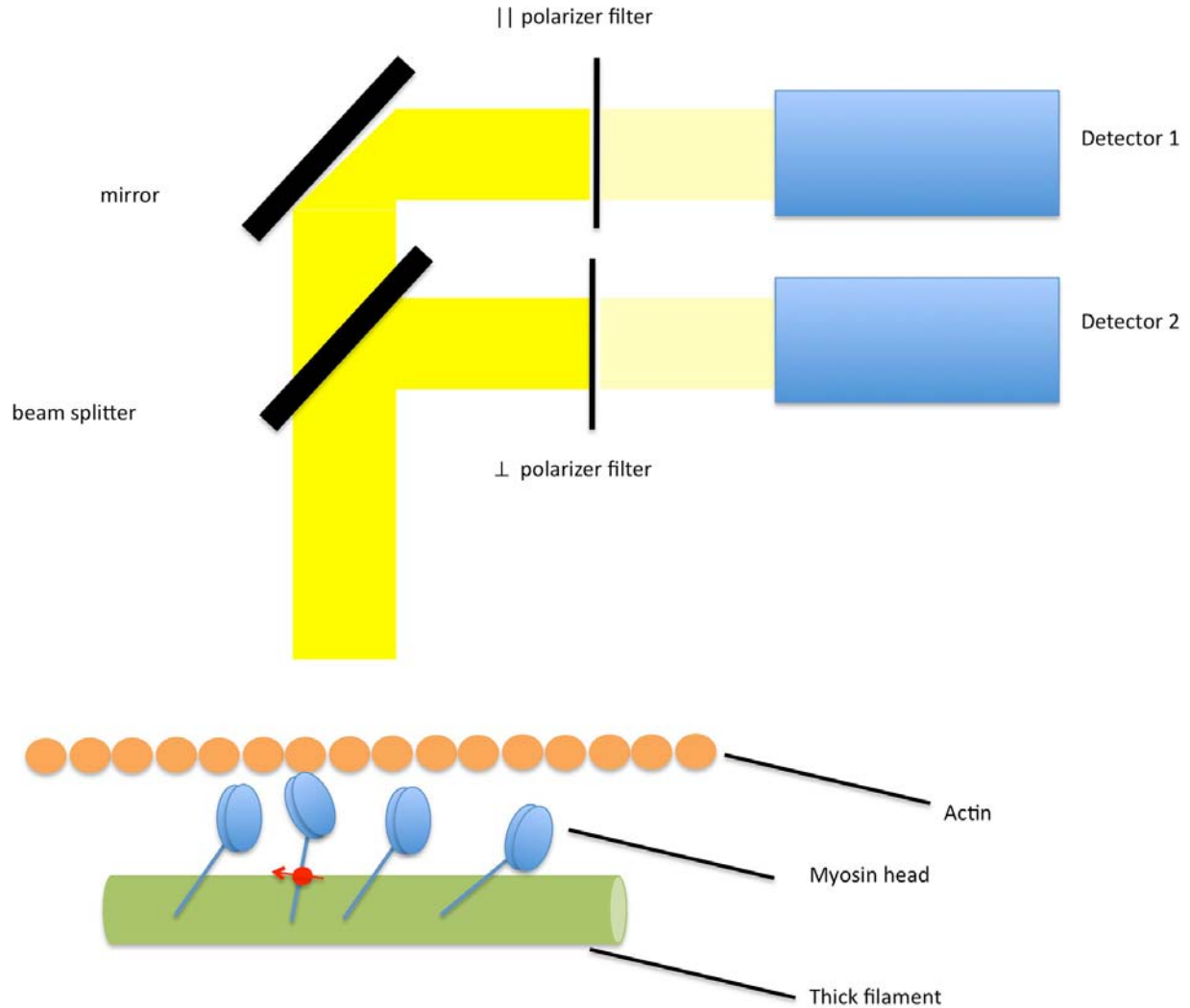


Figure 2. Measurement of dipole radiation from fluorescent molecule.

Two approaches may be taken at this point. First, we may treat the data as a single myosin simply by taking into account the number of myosin molecules in the sample. Second, we may treat the data as a *bulk* sample of an unknown number of myosin molecules. Each will employ a different spring constant, which we will see in the results below.

In the first case the standard deviation for both the velocity and position, respectively, are given as,

$$\sigma_v = \sqrt{1 - \frac{2}{\pi}} \sqrt{\frac{k_b T_{sample}}{N_{myosin} M}} \quad (5)$$

$$\sigma_x = \sqrt{1 - \frac{2}{\pi}} \sqrt{\frac{k_b T_{sample}}{N_{myosin} k}} \quad (6)$$

These distributions reflect the standard deviation treating the myosin as an individual. To treat the myosin in

bulk, there is no need to divide by the number of myosin in the sample yielding the following standard deviations for velocity and position respectively.

$$\sigma_v = \sqrt{1 - \frac{2}{\pi}} \sqrt{\frac{k_b T_{sample}}{M}} \quad (7)$$

$$\sigma_x = \sqrt{1 - \frac{2}{\pi}} \sqrt{\frac{k_b T_{sample}}{k}} \quad (8)$$

The initial position is given by a randomly selected position between the limits of the Gaussian weighted by the distribution.

Simulation model of myosin with experimental data

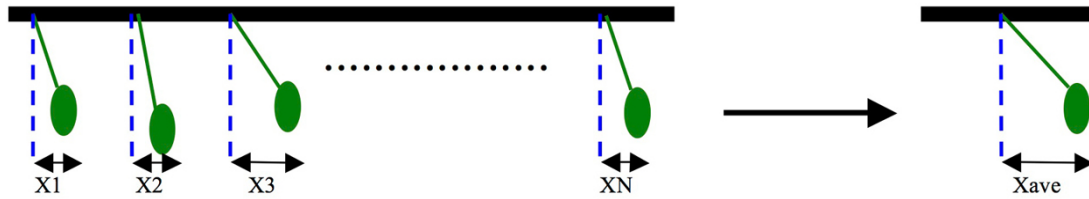


Figure 3. Superposition of myosin sample producing average position.

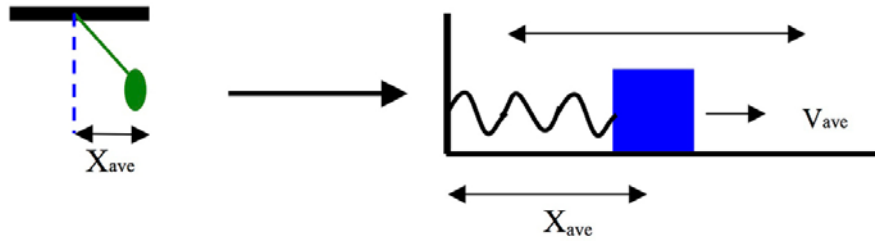


Figure 4. Average position of myosin sample translating to linear 1-D harmonic oscillator model.

$$x_{random} = P(x_i) \quad (9)$$

In addition to the random position, we also calculated an initial random velocity. The values are randomly selected between the limits of the Gaussian weighted by the distribution.

$$v_0 = P(v_i) \quad (10)$$

The ATP molecule supplies the energy required to displace the myosin and do work. Therefore, the position change due to that energy can be calculated from Hooke's law. Because the average position seems to be perturbed at random in either the positive or negative direction the sign is randomly selected.

$$x_{ATP} = \pm \sqrt{\frac{2E_{ATP}}{k}} P(v_0) \quad (11)$$

4. DATA INTERPRETATION

Because of the large number of data points a method of quantifying the data became necessary. A method of plotting the data and its best-fit linear line became the simplest approach for quantifying the data.

The output of the calculation is shown below. We have plotted the data and the best-fit line in a phase space plot (velocity versus position). From this we can visualize the distribution of the data and from the slope we can calculate how the physical properties of the myosin change under different conditions.

The velocity is given in meters per second (m/s), the x-position is given in meters (m), and the slope is given in inverse seconds (1/s). This slope could also be interpreted as an average frequency of oscillation.

The velocity of the myosin are calculated by taking the difference in position from one data point to the next and divided by the sample rate (sample rate = 0.01 seconds). This is not the true velocity of the myosin since we are not tracking the position of each myosin individually; rather we are calculating the velocity from the average position, which is random when measured. The velocity is calculated with the following expression.

$$v_i = \frac{x_i - x_{i-1}}{\Delta t} \quad (12)$$

Where v_i is the velocity of the i th data point, x_i is the i th x-position data point, x_{i-1} is the i th minus one data point, and Δt is a constant 0.01 seconds which is dictated by the sample rate of the data acquisition.

5. RESULTS

The outputs of the simulations are given in this section along with experimental data, for cardiac muscle, collected at the University of North Texas Health Science center by Dr. Julian Borejdo and Dr. Krishna Midde.

Plotting the slope calculated for each file per trial represents the data. In Figure 5, Figure 7, and Figure 8 the plots show 19 output files run 7 times to generate 133 simulated slopes plotted against 19 actual data files generating a single slope each. In Figure 6 and Figure 9 the plots show 26 output files run 7 times to generate 182 simulated slopes plotted against 26 actual data files generating a single slope each. The spread of simulated

Simulation model of myosin with experimental data

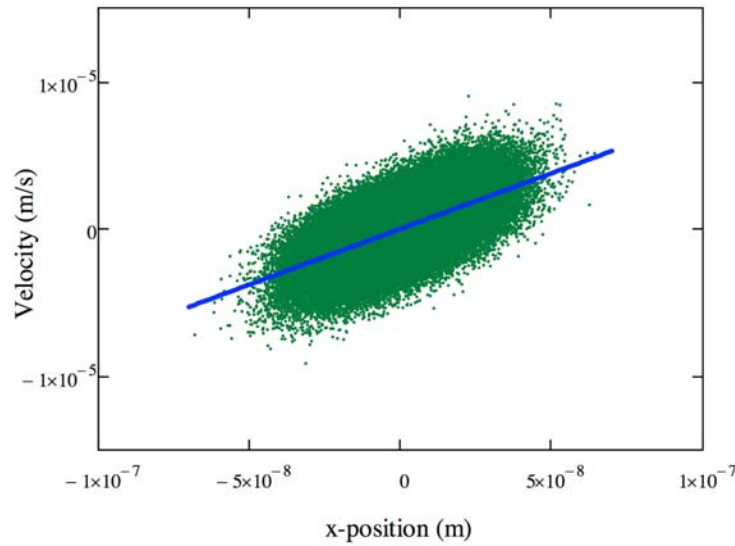


Figure 5. Phase space plot, velocity vs. x-position, of a myosin sample.

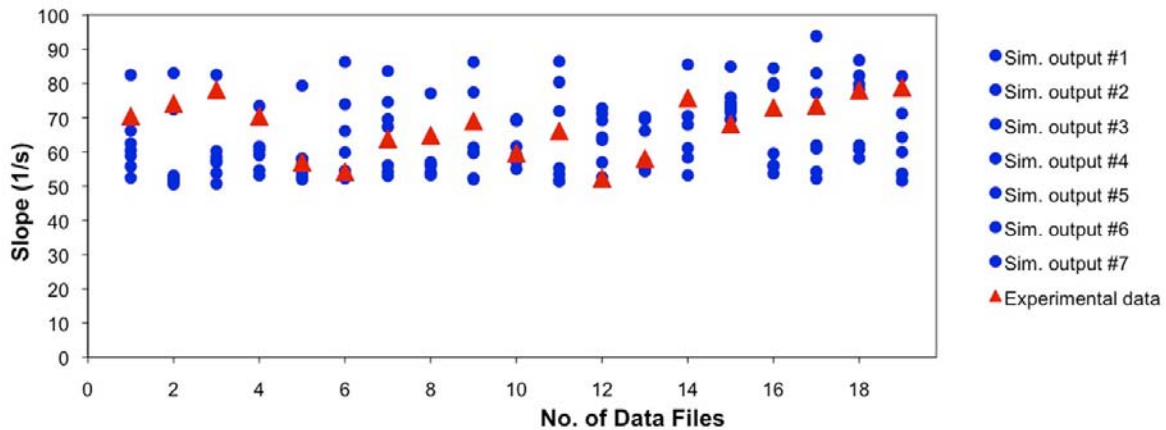


Figure 6. Simulation (Sim.) output (spring constant $k = 0.66$) and Phosphorylated relaxation experimental data.

data gives the range that you would expect the actual data to fall within given a spring constant.

Results and spring values when oscillators are accounted as a single myosin are shown in Figure 6, Figure 7, and Figure 8.

Results and spring values when oscillators are accounted for in *bulk* are shown in Figure 9, Figure 10, and Figure 11.

6. SIMULATION

Refer to section 9. MathCad Worksheet for the following description. The MathCad worksheet is divided into sections and each section is described below.

Input – The input section of the code consists of definitions of constants used in the calculations section; they are as follows.

A_0 – amplitude of the myosin, which is the maximum length that the myosin can reach.

M – mass of the myosin and cross-bridge combined.

N_{myosin} – number of myosin being simulated.

N_{files} – Number of files to be simulated.

T_{sample} – Temperature of sample.

k_b – Boltzmann's constant

k – spring constant of myosin.

E_{ATP} – is the energy released by ATP when it attaches itself to the myosin and breaks down into ADP.

Δt – sample rate of actual experiment.

Line #1 is a for-loop going from 0 to $N_{\text{files}}-1$ myosin being simulated. Line #2 is the random initial position for each of the myosin and line #3 is the random initial velocity. The fourth line is the for-loop that each myosin will go through to simulate one full cycle of a

Simulation model of myosin with experimental data

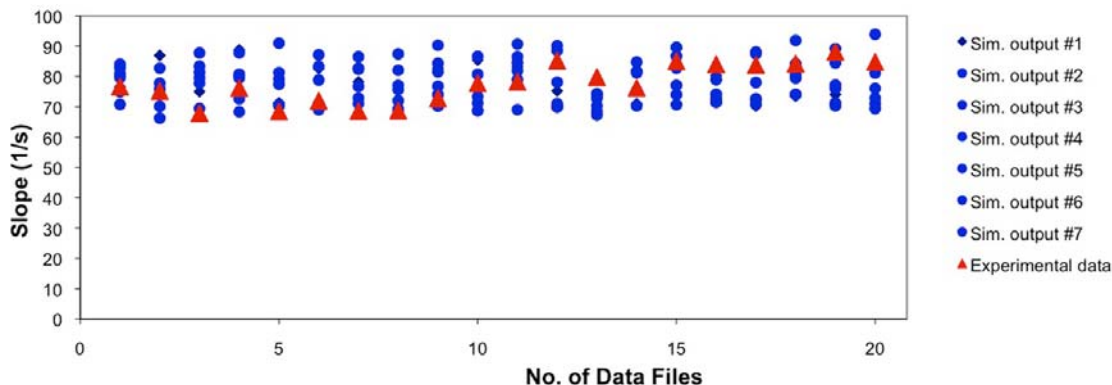


Figure 7. Simulation (Sim) output (spring constant $k = 0.32$) and Dephosphorylated relaxation experimental data.

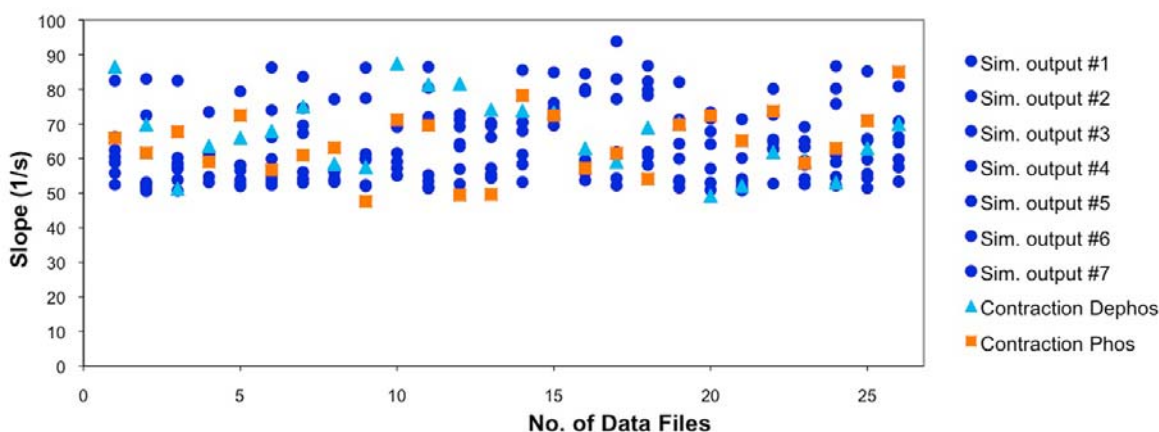


Figure 8. Simulation (Sim.) output (spring constant $k = 0.66$), Phosphorylated and Dephosphorylated contraction experimental data.

sinusoidal wave. Line #5 is a random number generator which outputs a number between 0 and 2π which will be used later to determine if the value of the random position shift due to the ATP will be positive or negative. Line #6 is the normal (Gaussian) distribution, which is the assumed distribution of values scaling the random shift in position which is then added to the position of the harmonic oscillator; the distribution is centered about the initial velocity (v_0). Line #7 is where the value from the velocity distribution is scaled by multiplying it by the maximum displacement due to the energy from ATP. Line #8 is the calculated position of the myosin, calculated by the solution of the harmonic oscillator and a random kick. The iteration number n is scaled by the inverse of the coefficient multiplied by 1000 seconds so that we get a range of values from 0 to 2π and cancels the dimensions. Line #9 stores the value for that iteration for each myosin building an array of values. Line #10 assigns the array to the variable x .

Next we calculate the velocity of the myosin. Line #1 is a for loop iterating through each myosin being simulated. Line #2 is the for-loop that each myosin will go through to simulate one full cycle of a sinusoidal wave. Line #3 where we calculate the velocity by taking the change in position from one element to the next and

dividing it by the change in time. Line #4 stores the value for that iteration for the velocity of each myosin building an array of values. Line #5 assigns the array to the variable v .

Now that we have arrays with values for the position and velocity of the myosin we want to calculate a best fit line for our data when we plot the position and velocity in a phase space plot (v vs. x). In line #1 we are iterating through each array of data for each of the myosin. Line #2 I calculate the slope (velocity/position) for each of the myosin. And in the remaining two lines I store each slope as an element of an array and assign it to the variable $mySlope$. The same is done for calculating the y-intercept.

The results for the slope and y-intercept are then averaged below in the first two lines. Then a range for the best-fit line is defined and finally the values for the best-fit line are computed.

In the error analysis section we compute the R2 deviation and the standard deviation of the data from the best-fit line. First we calculate the best-fit line for each of the data sets for each of the myosin. Then the R2 deviation is computed for each of the data sets for each of the myosin. Then the mean value for the R2 deviation is

Simulation model of myosin with experimental data

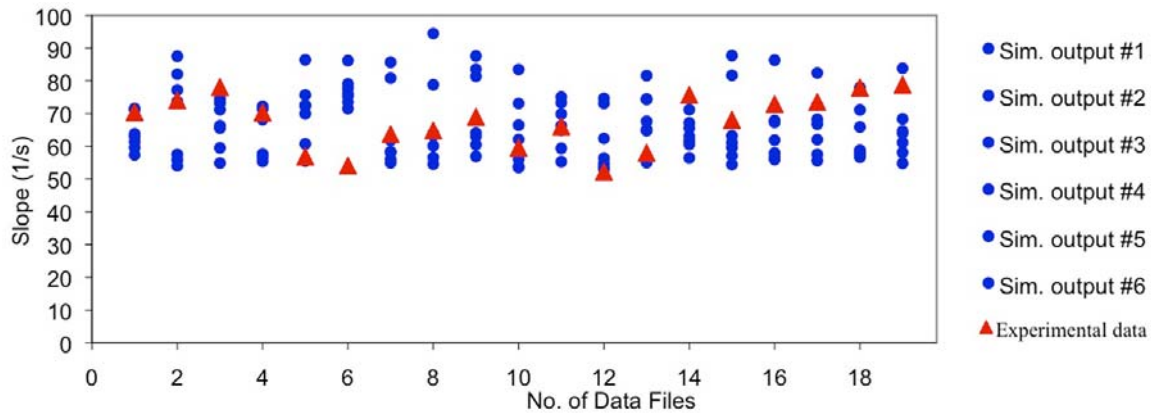


Figure 9. Simulation (Sim.) output (spring constant $k = 7.2$) and Phosphorylated relaxation experimental data.

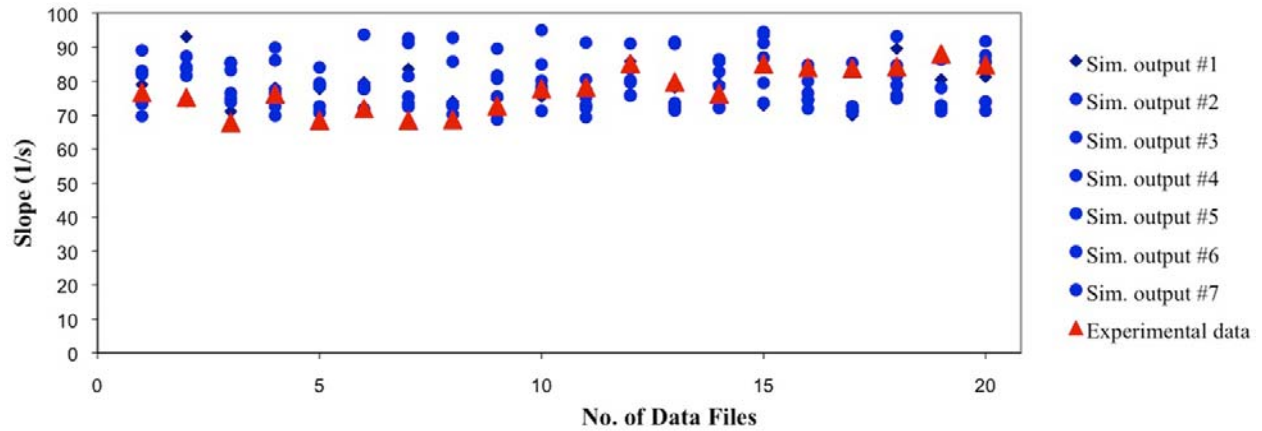


Figure 10. Simulation (Sim.) output (spring constant $k = 3.5$) and Dephosphorylated relaxation experimental data.

computed. Below that we compute the standard deviation of the slope and y-intercept values calculated above.

Output – The output of the calculation is shown below. We have plotted the data and the best-fit line in a phase space plot. From this we can visualize the distribution of the data and from the slope we can calculate how the physical properties of the myosin change under different conditions.

7. DERIVATION OF THEORETICAL MODEL

To calculate the standard deviation for the velocity distribution we must calculate the average velocity and the square of the average velocity.

$$\frac{\int_0^{\infty} v e^{-\frac{N_{\text{myosin}} M}{2k_b T_{\text{sample}}} v^2} dv}{\int_0^{\infty} e^{-\frac{N_{\text{myosin}} M}{2k_b T_{\text{sample}}} v^2} dv} = \sqrt{\frac{2k_b T_{\text{sample}}}{\pi N_{\text{myosin}} M}} \quad (13)$$

$$\overline{v^2} = \frac{\int_0^{\infty} v^2 e^{-\frac{N_{\text{myosin}} M}{2k_b T_{\text{sample}}} v^2} dv}{\int_0^{\infty} e^{-\frac{N_{\text{myosin}} M}{2k_b T_{\text{sample}}} v^2} dv} = \frac{k_b T_{\text{sample}}}{N_{\text{myosin}} M}$$

$$\overline{v^2} = \frac{\int_0^{\infty} v^2 e^{-\frac{N_{\text{myosin}} M}{2k_b T_{\text{sample}}} v^2} dv}{\int_0^{\infty} e^{-\frac{N_{\text{myosin}} M}{2k_b T_{\text{sample}}} v^2} dv} = \frac{k_b T_{\text{sample}}}{N_{\text{myosin}} M} \quad (14)$$

Next we calculate the standard deviation for the initial velocity spread, shown below.

$$\sigma_v = \sqrt{\overline{v^2} - \overline{v}^2} \quad (15)$$

$$\sigma_v = \sqrt{\frac{k_b T_{\text{sample}}}{N_{\text{myosin}} M} - \frac{2k_b T_{\text{sample}}}{\pi N_{\text{myosin}} M}} \quad (16)$$

Simulation model of myosin with experimental data

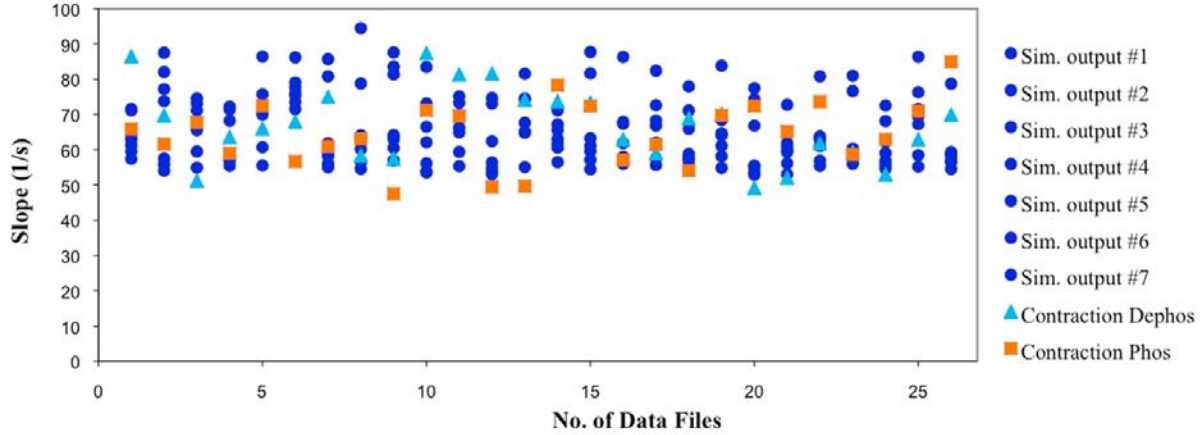


Figure 11. Simulation (Sim.) output (spring constant $k = 7.2$), Phosphorylated and Dephosphorylated contraction experimental data.

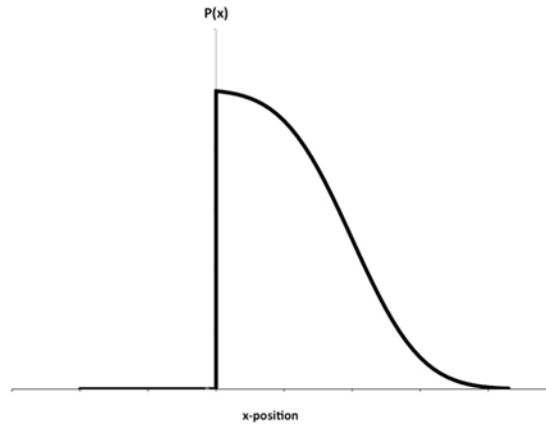


Figure 12. Probability distribution for position of myosin

$$\sigma_v = \sqrt{1 - \frac{2}{\pi} \sqrt{\frac{k_b T_{sample}}{N_{myo \sin} M}}} \quad (17)$$

To calculate the standard deviation for the position distribution we must calculate the average position and the square of the average position.

$$\bar{x} = \frac{C \int_0^{\infty} x e^{-\frac{N_{myo \sin} k}{2k_b T_{sample}} x^2}}{C \int_0^{\infty} e^{-\frac{N_{myo \sin} k}{2k_b T_{sample}} x^2}} = \sqrt{\frac{2k}{\pi \Lambda}} \quad (18)$$

$$\bar{x}^2 = \frac{C \int_0^{\infty} x^2 e^{-\frac{N_{myo \sin} k}{2k_b T_{sample}} x^2}}{C \int_0^{\infty} e^{-\frac{N_{myo \sin} k}{2k_b T_{sample}} x^2}} \quad (19)$$

The reason for integrating from 0 to infinity is because the actual myosin start at an initial position swing out to a maximum position and then return to its starting position and not passed. Therefore, the probability of finding the myosin behind its starting position is zero. See Figure 12.

Next we calculate the standard deviation for the initial position spread, shown below.

$$\sigma_x = \sqrt{\bar{x}^2 - x^2} \quad (20)$$

$$\sigma_x = \sqrt{\frac{k_b T_{sample}}{N_{myo \sin} k} - \frac{2k_b T_{sample}}{\pi N_{myo \sin} k}} \quad (21)$$

Simulation model of myosin with experimental data

$$\sigma_x = \sqrt{1 - \frac{2}{\pi} \sqrt{\frac{k_b T_{sample}}{N_{myo \sin} k}}} \quad (22)$$

The initial position and velocity distribution are then given by,

$$P(v) = \frac{e^{\frac{-1}{2} \sqrt{1 - \frac{2}{\pi} \sqrt{\frac{N_{myo \sin} M}{k_b T_{sample}}} v^2}}}{\sqrt{1 - \frac{2}{\pi} \sqrt{\frac{k_b T_{sample}}{N_{myo \sin} M}}} \sqrt{2\pi}} \quad (23)$$

$$P(x) = \frac{e^{\frac{-1}{2} \sqrt{1 - \frac{2}{\pi} \sqrt{\frac{N_{myo \sin} k}{k_b T_{sample}}} x^2}}}{\sqrt{1 - \frac{2}{\pi} \sqrt{\frac{k_b T_{sample}}{N_{myo \sin} k}}} \sqrt{2\pi}} \quad (24)$$

The derivation for the motion of the oscillator is as follows. We know from Hooke's law that the force is given by,

$$F = -kx = M \frac{d^2 x}{dt^2} \quad (25)$$

We can rewrite this as follows,

$$\frac{d^2 x}{dt^2} + \frac{k}{M} x = 0 \quad (26)$$

Which has the general solution,

$$x(t) = A_0 \sin(\omega t) + C \quad (27)$$

Where,

$$\theta = \omega t \quad (28)$$

$$\omega = \sqrt{\frac{k}{M}} \quad (29)$$

And at $t = 0$ the constant is,

$$C = x_{ATP} + x_{random} \quad (30)$$

Which gives the final solution,

$$x(\theta) = A_0 \sin(\theta) + x_{ATP} + x_{random} \quad (31)$$

8. CONCLUSION

From the results presented above there is good agreement between the experimental data collected and the range of data points predicted by the theoretical model. As seen above, a simple classical 1-D harmonic oscillator model is sufficient to model the behavior of the myosin. As the number of myosin molecules in the sample becomes greater than one, further application of Brownian motion and Maxwell-Boltzmann statistics are needed to predict the average behavior. Improving the agreement between the theoretical and experimental data can be achieved by measuring more accurately the temperature of the sample and routine calibration of experimental equipment.

We also see from the data presented above that the theoretical model can be used to study the effect of phosphorylation on myosin. A further application of this method of data interpretation would be in identifying individuals with Familial Cardiac Hypertrophy by comparing the results from healthy individuals, individuals with the disorder, and individuals whose result is unknown to determine whether or not they have the disorder.

The current model does not describe the low ATP case, further development of the model is needed to add the dependence of the quantity of ATP present. Also, further study is needed to compare this model with fluorescence data for the pre and post contraction states. If you look at the distribution of points for the Phosphorylated data in Fig 9 the wider distribution of points in the Phosphorylated data may suggest that a number of the myosin have entered the pre-power stroke. Our future work, current work in progress, will accommodate for ATPase activity and power stroke states.

9. MATHCAD WORKSHEET

The Input, calculations, calculation of velocity, calculation of best fit line, results of best fit line, error analysis of best fit line and plots are presented in figures 13 - 18.

Simulation model of myosin with experimental data

INPUT

$A_0 := 10 \cdot 10^{-9} \cdot \text{m}$	Amplitude	$k_b := 1.38 \cdot 10^{-23} \cdot \frac{\text{m}^2 \cdot \text{kg}}{\text{s}^2 \cdot \text{K}}$	Boltzmann constant
$M := 2.32 \cdot 10^{-22} \cdot \text{kg}$	Mass	$k := 0.32 \cdot 10^{-3} \cdot \frac{\text{N}}{\text{m}}$	Spring constant
$N_{\text{myosin}} := 12$	Number of myosin	$E_{\text{atp}} := \frac{20500}{6.022 \cdot 10^{23}} \cdot \text{J}$	Energy delivered by ATP
$N_{\text{files}} := 27$	Number of files	$\Delta t := 0.01 \cdot \text{s}$	Change in time (sample rate)
$T_{\text{sample}} := 291.5 \cdot \text{K}$	Temp of sample		

Figure 13. Input.

CALCULATIONS

$$\sigma_v := \sqrt{1 - \frac{2}{\pi}} \cdot \sqrt{\frac{k_b \cdot T_{\text{sample}}}{N_{\text{myosin}} \cdot M}} \quad \text{Standard deviation of velocities}$$

$$\sigma_x := \sqrt{1 - \frac{2}{\pi}} \cdot \sqrt{\frac{k_b \cdot T_{\text{sample}}}{N_{\text{myosin}} \cdot k}} \quad \text{Standard deviation of start position}$$

Calculate Positions

```

x := for i ∈ 0..(N_files - 1)                                     1
    |
    | x_0 ← rnorm(1, 0, σ_x · 1/m)                               2
    | v_0 ← rnorm(1, 0, σ_v · s/m)                               3
    | for n ∈ 0..6280                                           4
    | | R ← rnd(2 · π)                                           5
    | | S ← rnorm(1, v_0, σ_v · s/m)                             6
    | | x_atp ← if(R < π, S_0 · √(2 · E_atp / k), -S_0 · √(2 · E_atp / k)) 7
    | | A ← A_0 · sin(n · s / (10^3 · s)) + x_atp + x_0 · m    8
    | | B_{n,i} ← A                                             9
    | C_n ← B                                                  10

```

Figure 14. Calculations.

Calculate Velocity

```

v := | for i ∈ 0..(Nfiles - 1)           1
      | for n ∈ 1..6280                 2
      | | (x<i>)n - (x<i>)n-1         3
      | | A ← -----
      | | Δt
      | | Bn,i ← A                     4
      | Ci ← B                         5

```

Calculate Best Fit Line

```

mySlope := | for i ∈ 0..(Nfiles - 1)   1
            | | G ← slope(x<i>,v<i>)    2
            | | Mi ← G                 3
            | M                          4

```

Calculate slope

```

yIntercept := | for i ∈ 0..(Nfiles - 1) 1
               | | H ← intercept(x<i>,v<i>) 2
               | | Mi ← H                 3
               | M                          4

```

Calculate y-intercept

Figure 15. Calculation of velocity and best fit line.

Results of Best Fit Line

$\text{mean}(\text{mySlope}) = 75.611 \frac{1}{\text{s}}$ Calculate an average slope from each data file

$\text{mean}(\text{yIntercept}) = 3.597 \times 10^{-9} \frac{\text{m}}{\text{s}}$ Calculate an average y-intercept from each data file

$\text{polRange} := -7 \cdot 10^{-8} \cdot \text{m}, -6.9 \cdot 10^{-8} \cdot \text{m} .. 7 \cdot 10^{-8} \cdot \text{m}$ Define range that best fit line will be plotted

$\text{bestFitLine}(\text{polRange}) := \text{mean}(\text{mySlope}) \cdot \text{polRange} + \text{mean}(\text{yIntercept})$ Calculate points for best fit line.
Y = mX + b

Figure 16. Results of best fit line.

Error Analysis of Best Fit Line

```

bestFit := for i ∈ 0..(Nfiles - 1)           1
           | I ← mySlopei · x(i) + yIntercepti       2
           | Mi ← I                               3
           | M                                       4
           M
R2 := for i ∈ 0..(Nfiles - 1)           1
      | J ← corr(v(i), bestFiti)                 2
      | Mi ← J                               3
      | M                                       4
      M
mean(R2) = 0.614
stdev(mySlope) = 5.427  $\frac{1}{s}$ 
stdev(yIntercept) = 3.801 × 10-8  $\frac{m}{s}$ 
    
```

Calculate best fit line for each data file and calculate the R-squared deviation for each.

Calculate mean of R-squared deviation for each data file.

Calculate standard deviation of slope for each file.

Calculate standard deviation of y-intercept for each file.

Figure 17. Error analysis of best fit line.

PLOTS

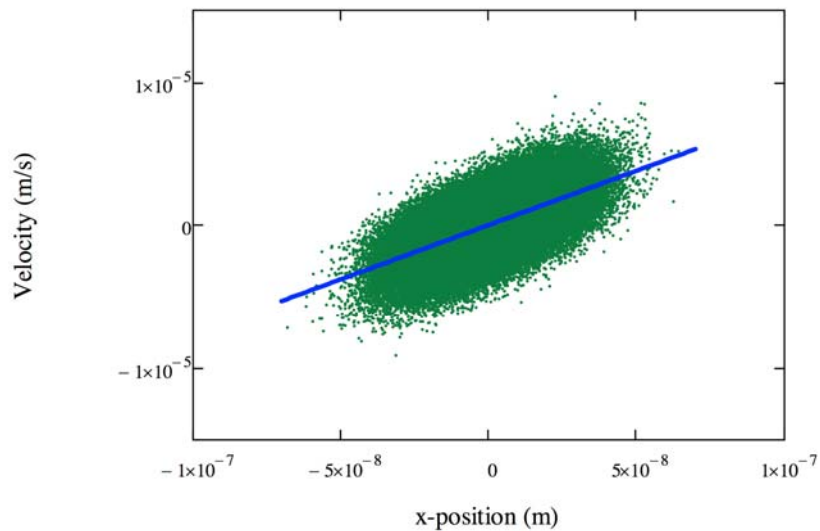


Figure 18. Plots.

10. ACKNOWLEDGMENTS

I would like to thank Dr. Julian Borejdo at the University of North Texas Health Science Center in the department of molecular biology and Dr. Krishna Midde for offering the data they collected to compare with the theoretical predictions made in this paper; also, for their assistance in editing this paper in preparation for publication. I would also like to thank Stephanie Tziavaras

and Kenny Leeson for their donations to help publish this work.

11. REFERENCES

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Simulation model of myosin with experimental data

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