User-guide for TPM GUI

Brief overview

The GUI was developed using MATLAB® version 2022b. Compatibility with other versions was not tested. Some routines run into errors if the user input is incorrect. Commonly encountered errors and how to avoid them are described in this document. The GUI simulates the x,y, and z position of a tethered particle as found in tethered particle motion (TPM) experiments. In addition to the position, the forces acting on the system (external applied force and total force) are simulated. The plot update rate (PPP) affects the performance significantly. It is advised to begin using the GUI with the default values. Basic MATLAB skills are needed to use the GUI.

Graphical User Interface

GUI layout

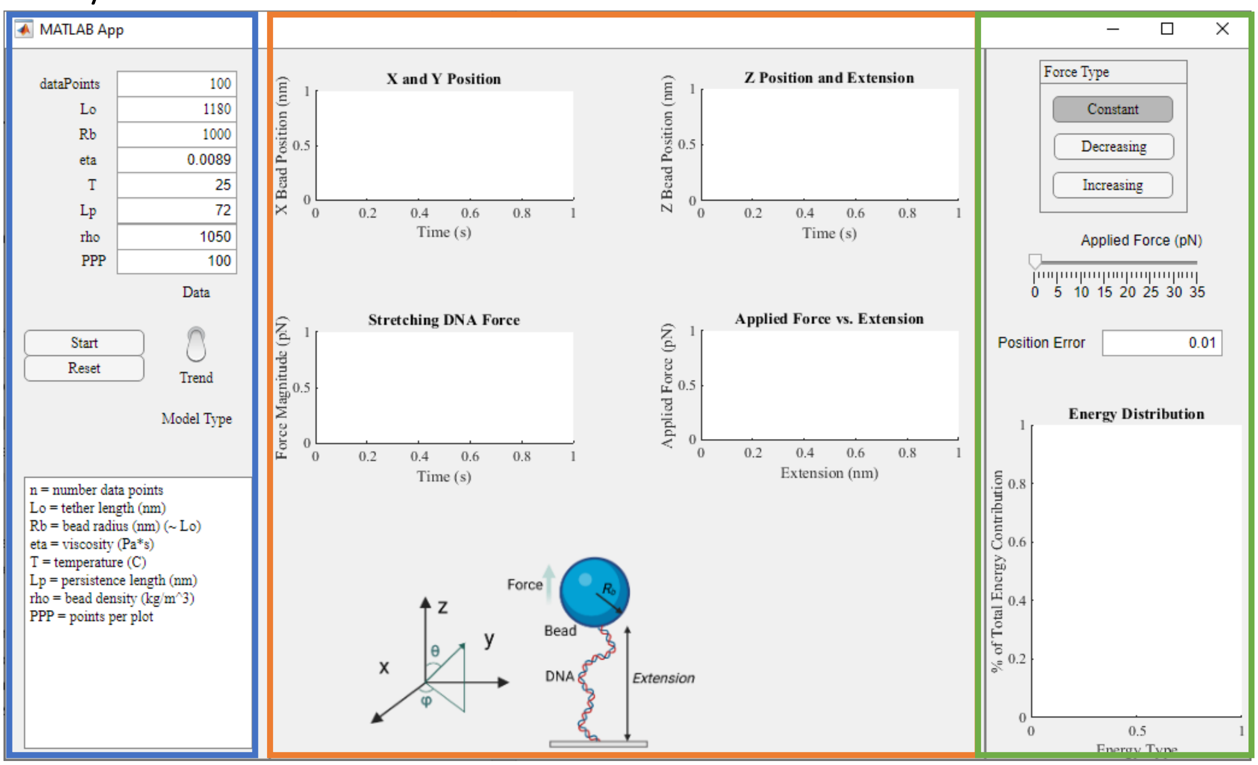

Figure 1: GUI overview and descriptions.

Figure 1 shows the GUI after startup. The section framed in blue (left) contains a list of variables which the user can modify; a description of each is found at the bottom of the section. The start button initiates the TPM simulation, whereas the reset button clears the workspace. The toggle switch allows the user to switch between two simulation types: 1) Data and 2) Trend, see section Model descriptions. The GUI does not have a stop button and the user will need to abort execution in the MATLAB command window by pressing “Ctrl+C”. Depending on the state of the simulation, “Ctrl+C” needs to be pressed more than once to fully exit the simulation. Simulation data will not be saved if simulation is aborted.

The orange framed section (middle) displays the position and forces of the TPM simulation and a corresponding sketch. The force is currently only applied in z, but the code can be expanded to include a force application in x/y.

The green section (right) contains the force application mode: 1) constant, 2) decreasing, 3) increasing along with a slider to apply the force in z. While the constant button is pressed, the force is applied for the whole duration of the simulation at the value specified by the force slider. In contrast, the decreasing and increasing buttons create a linearly decreasing or increasing force during the duration of the simulation, with the maximum force being set by the slider and the minimum force being zero. The field position error relates to the constraint model (see section Model descriptions). The conservation of energy is displayed as a set of bar graphs that show potential and kinetic energy, respectively. This allows the user to quickly verify if the input parameters (such as viscosity) were physically reasonable and resulted in a dominance of potential over kinetic energy.

Model descriptions

The GUI uses two models for the simulation: 1) Data and 2) Trend as set by the toggle switch. The Data simulation is based on a physical description of tethered particle motion as described in the main of the publication (equations 1-16). The Trend model is a hybrid between the Data model and a constrained model based on a Markov process. The advantage of the Data model is that it obeys the probabilistic description of the TPM system, but can fail if large force jumps from one simulation point to the next occur. In some situations, the simulation is also slower than the hybrid model. In contrast, the Trend model switches between the probabilistic and the constrained simulation and as such the simulation output (position, forces, etc.) contains a larger errors in the force and position estimation, but runs more stable and, in general, faster than the Data model. Nevertheless, it perfectly captures any trends of the system, e.g. a reduction in fluctuations when the force is increased in a typical force-extension experiment. A randomly chosen parameter called “Position Error” can be adjusted to more closely match the constrained model to the probabilistic model and mainly influences the time scale. The default value of 0.01 works well for most TPM scenarios.

Starting the GUI

Unpack the zip file and open “TPMGUI.mlapp” as shown in Figure 2.

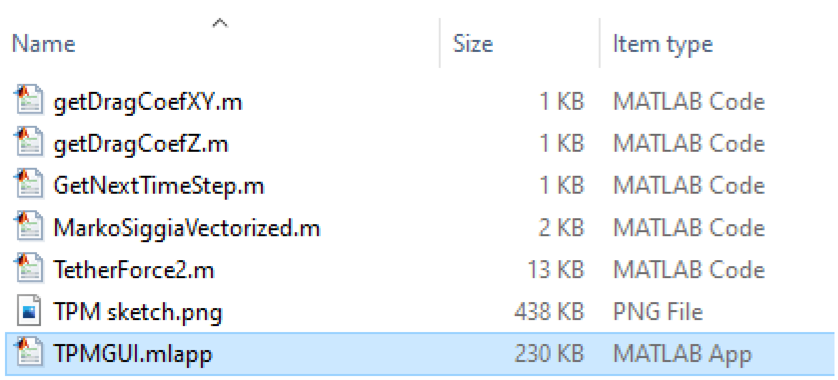

Figure 2: Opening the GUI.

MATLAB opens alongside the GUI and by default the active folder contains all subfunctions needed to run the GUI as shown in Figure 3.

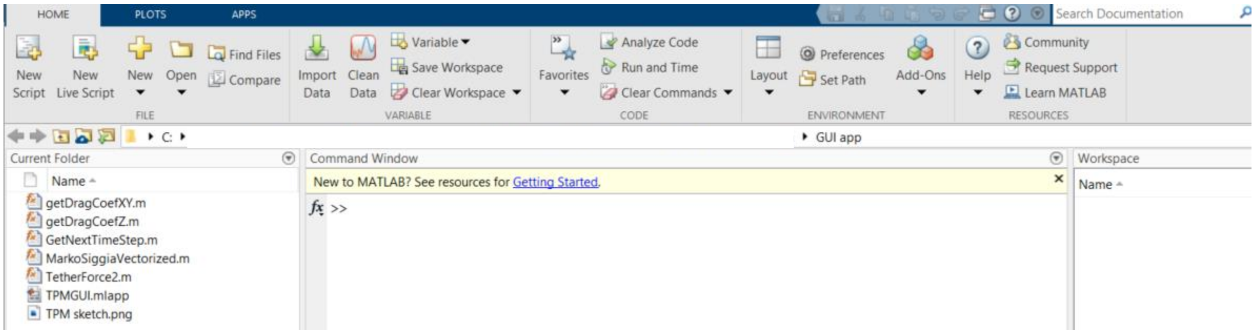

Figure 3: MATLAB window showing the current folder.

In parallel, the GUI opens up as a separate window as shown in Figure 1 and is ready to use.

Example 1: Simulation with a constant force turned on, off and modified during simulation

After starting the GUI, keep all parameters as default except “dataPoints”, which is set to 1000, “PPP” set to 10 and “Data” mode. This means that the simulation will contain 1000 data points and all plots will be updated every 10 computations. These settings will simulate less than one minute of data, where the user can manually apply forces to the TPM system.

1. Begin by pressing the “Start” button, watch as the graphs in the middle sections begin to display the simulation output.
2. Use the force slider on the right to apply a force and watch how the bead is being “pulled up” from the surface as indicated by a rise in the z position.
3. Move the force slider back to zero and watch how the bead “drops” back to the surface.
4. Repeat the force application for various forces until the end of the simulation.
5. At the end of the simulation, a pop-up window will appear that prompts the user to save the data as shown in Figure 4 (red arrow).
6. Enter a file name and press OK. The simulation data will be saved as a csv file in the same folder where the GUI is located.
7. After saving the data, the GUI updates the energy distribution bar plot. For a “realistic” simulation, the potential energy (PE) should be significantly larger than the kinetic energy (KE) as seen in Figure 5.
8. Press the “Reset” button and repeat the simulation with more data points, or vary the bead radius or tether length.

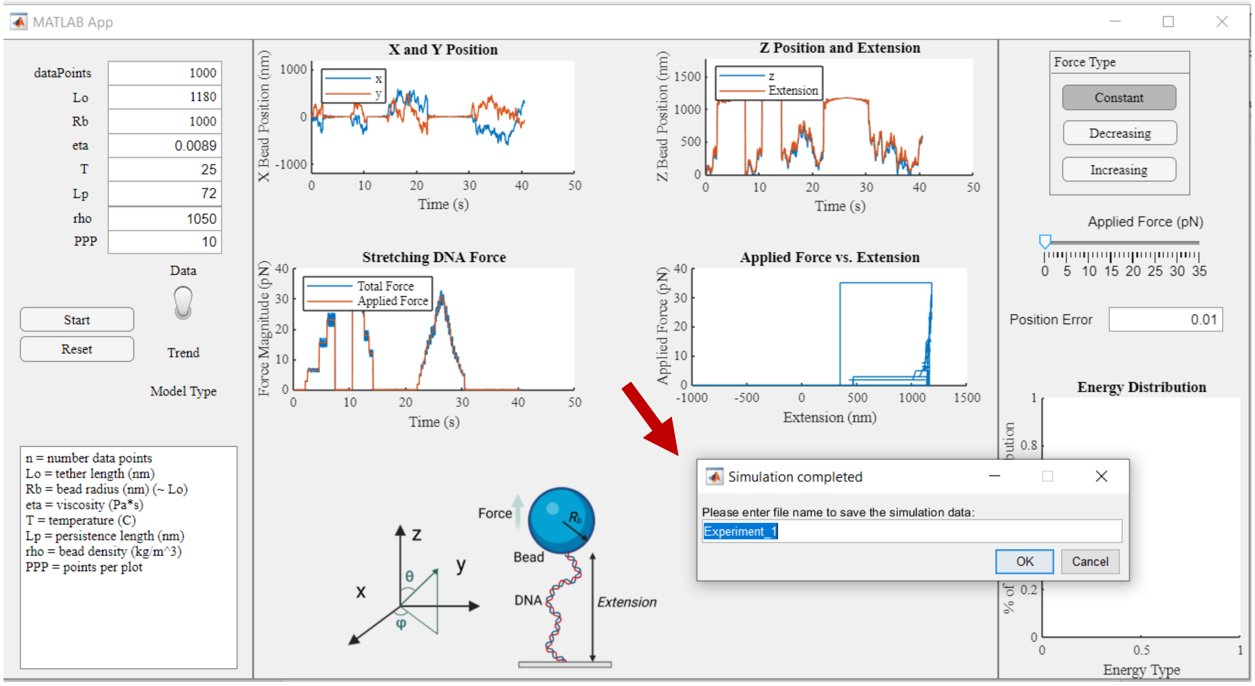

Figure 4: GUI after constant force simulation. After completion of the simulation, a pop-up window will appear (indicated by the red arrow) that prompts the user to specify a file name and save the simulation data.

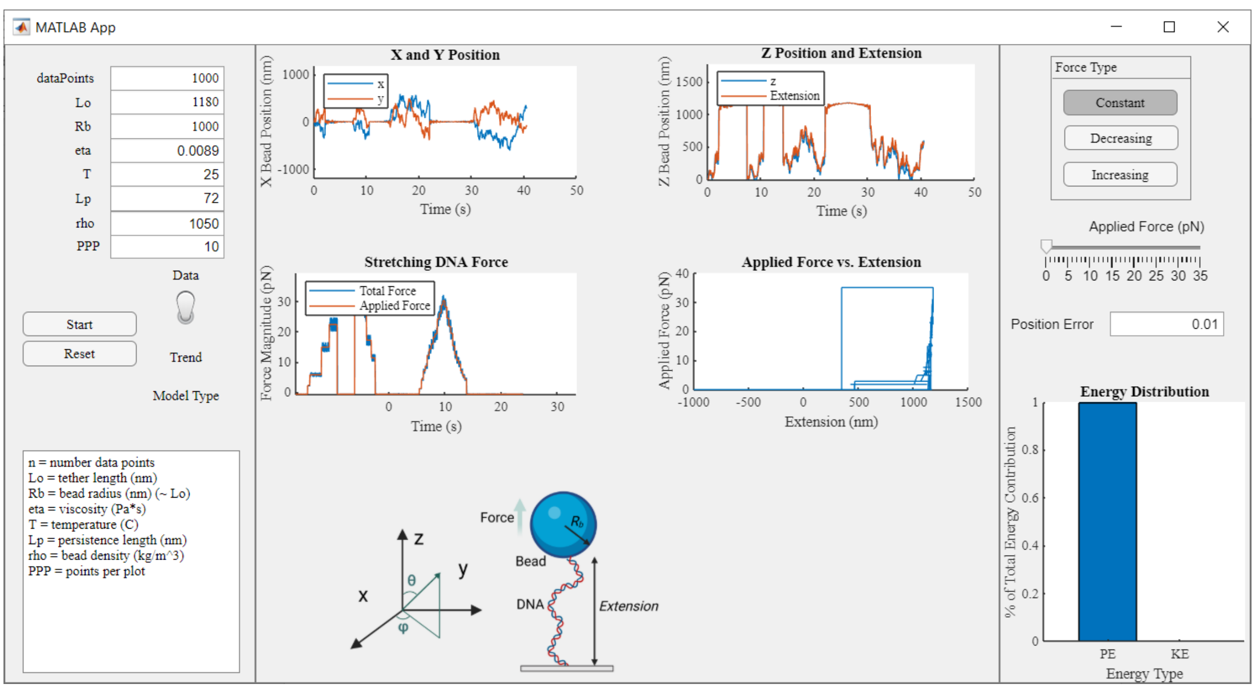

Figure 5: After saving the simulation data, the GUI will update the energy distribution on the right panel of the GUI. The potential energy (PE) should dominate the kinetic energy (KE) for a realistic TPM simulation.

Example 2: Simulation with linear force ramp in Data and trend model

This example illustrates the differences between the two simulation models. Keep all parameters set as in Example 1.

1. Toggle the switch to “Data” model.
2. Set the force slider to the maximum value (35 pN).
3. Press the button “Increasing”.
4. Press start and save the data if needed.
5. The simulation should look like as shown in Figure 7.
6. Press reset and toggle the switch to the “Trend” model.
7. Press start and save the data if needed.
8. The simulation should look like as shown in Figure 7.

The force extension trend looks similar for both model types, but the biggest difference is in the total estimated force as well as the x and y fluctuations.

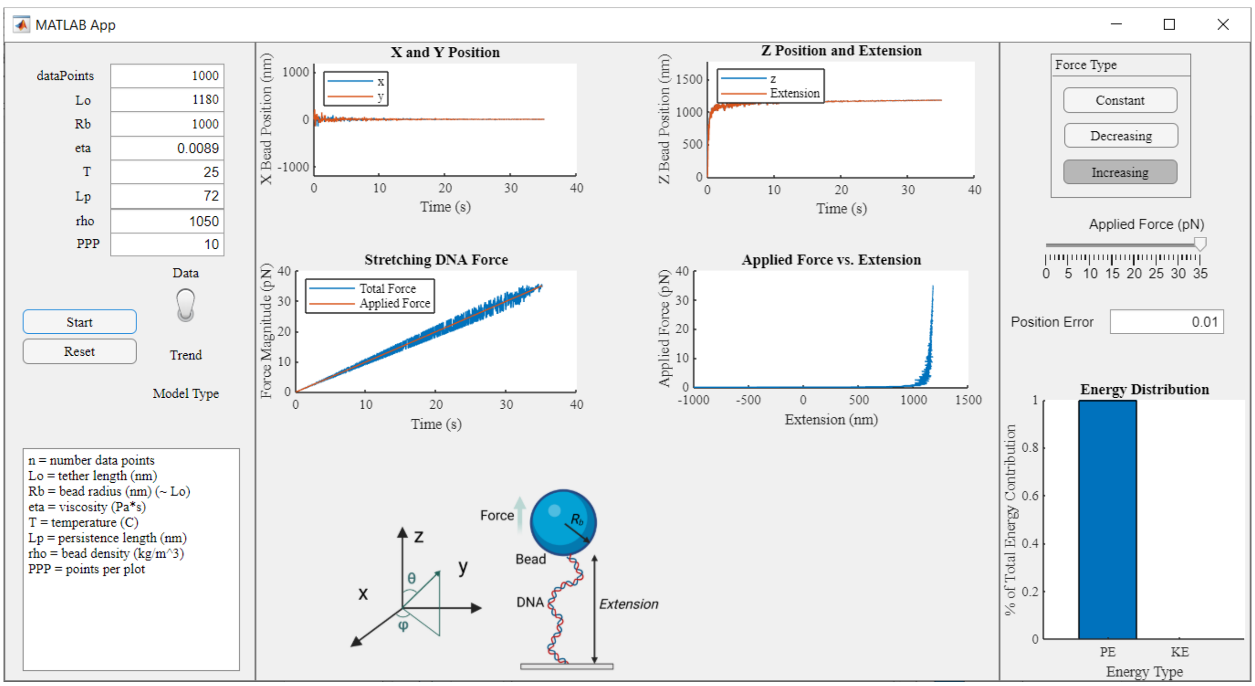

Figure 6: GUI after running a linearly increasing force ramp using the Data model.

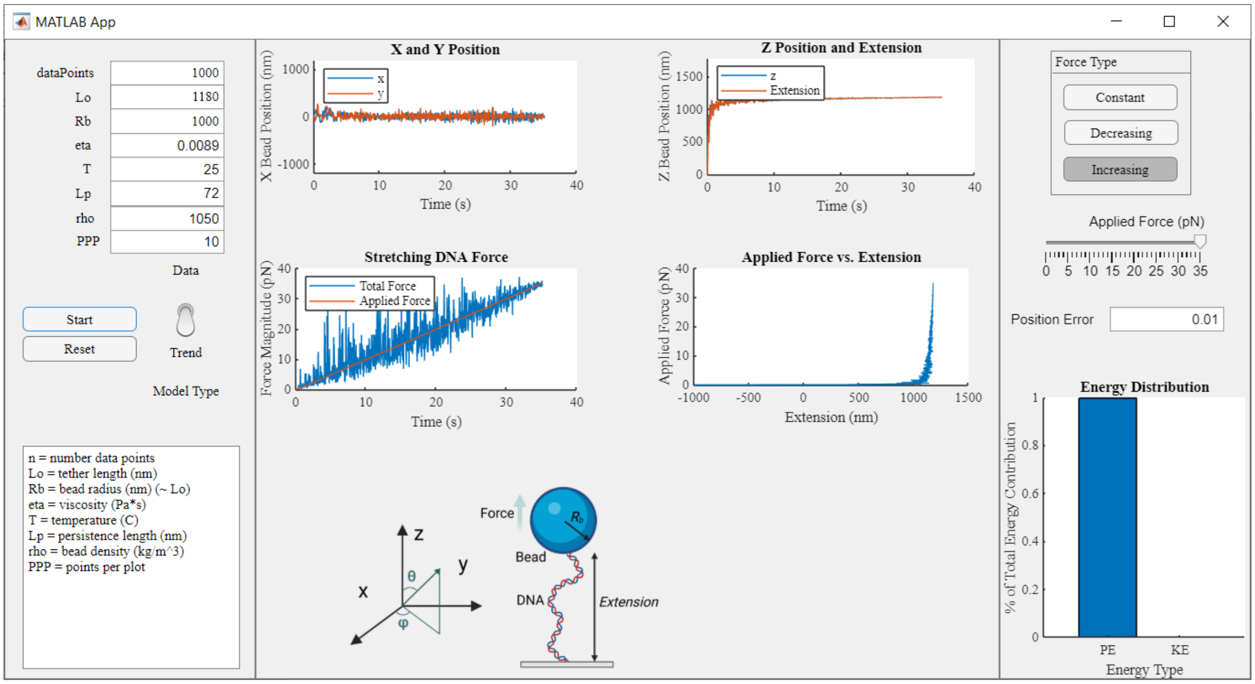

Figure 7: GUI after running a linearly increasing force ramp using the Trend model.

Common Errors

Persistence length and applied force

The model is sensitive to the input parameters and some internal functions yield fatal errors. For example, if the persistence length (Lp) is set too small, then the simulation will run into an error solving for the force as shown in Figure 8 and Figure 9 if the applied force is too large.

1. In either Data or Trend mode, set Lp to 20 (nm).
2. Set the force button to constant.
3. Set the force slider to 0.
4. Start the simulation.
5. Increase the force to 5 pN, simulation should continue.
6. Increase the force to 15 pN, simulation should continue.
7. Increase the force to 25 pN, simulation should stop and error message in Figure 9 appear.

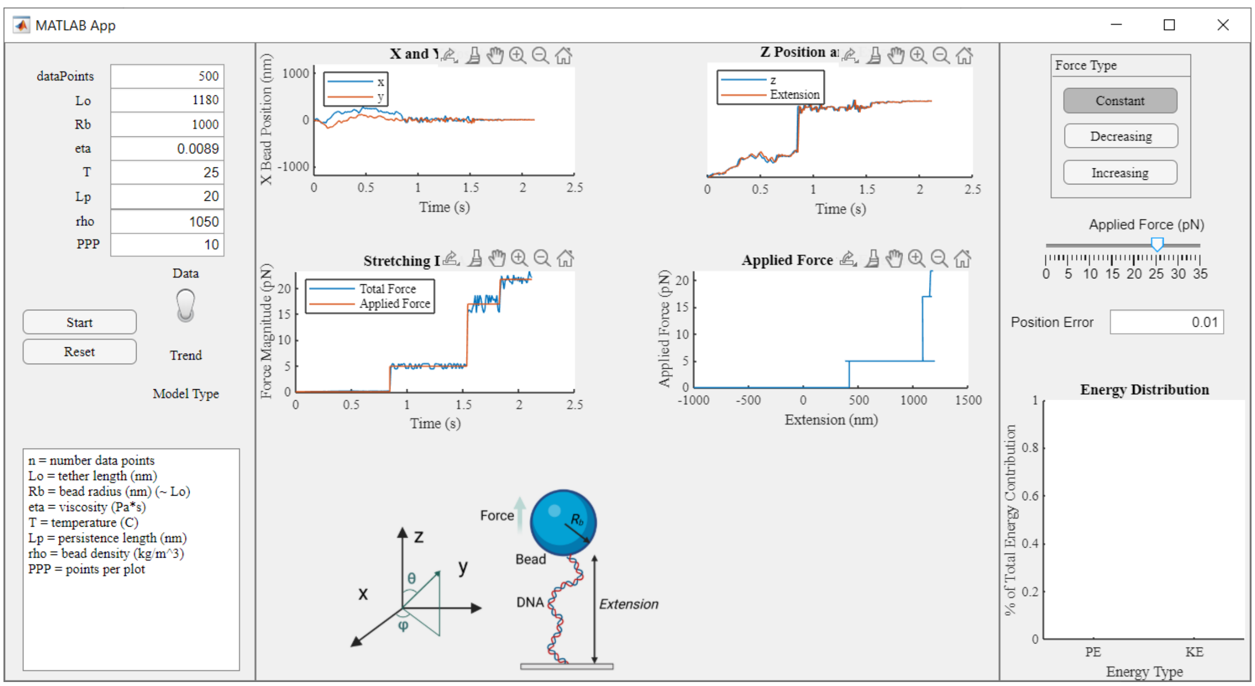

Figure 8: Example of error. A low persistence length results in errors solving for the force.

```
Error using fzero
Initial function value must be finite and real.

Error in MarkoSiggiaVectorized (line 24)
tempForcez = fzero(tempFuncz,1e-14);

Error in TetherForce2>RandWalkSim (line 255)
        DNAForceX = MarkoSiggiaVectorized(kbT, Lp, Lo, extensionX,extensionY,extensio

Error in TetherForce2 (line 14)
[Xsim,Ysim,Zsim, FullExtension, AngleSimThetaDegree, AngleSimPhiDegree, DNAForce, tim

Error in TPMGUI/StartButtonPushed (line 172)
            [t,df,x,y,z,extension,dfx,dfy,dfz,theta,phi]=TetherForce2(forceArray(1+i-

Error in appdesigner.internal.service.AppManagementService/executeCallback (line 138)
                callback(appOrUserComponent, event);

Error in matlab.apps.AppBase>@(source,event)executeCallback(appdesigner.internal.serv
            newCallback = @(source, event)executeCallback(appdesigner.internal.servic

Error using matlab.ui.control.internal.controller.ComponentController/executeUserCall
Error while evaluating Button PrivateButtonPushedFcn.

fx >>
```

Figure 9: Error codes when the persistence length is set too small. The MATLAB function "fzero" returns an error and stops the simulation.

Saving data

After a successful simulation, the user is asked to save the data. If "Cancel" is pressed, then the error shown in Figure 10. Note that this error can be mitigated by checking if the variable "answer" is empty or not. If a file already exists with the name that the user had specified, then the original file will be overwritten with the most recent simulation data.

```
Error in TPMGUI/StartButtonPushed (line 318)
       str=append(answer{1},'.csv');

Error in matlab.apps.AppBase>@(source,event)executeCallback(appdesigner.internal.serv
            newCallback = @(source, event)executeCallback(appdesigner.internal.servic

Error while evaluating Button PrivateButtonPushedFcn.

fx >>
```

Figure 10: Error after pressing "Cancel" at the save data pop-up window.

Case of kinetic energy dominating

As mentioned in the publication, the simulation is valid, if the potential energy (PE) dominates. Typically, kinetic energy dominates, if low values for the viscosity are set as shown in Figure 11.

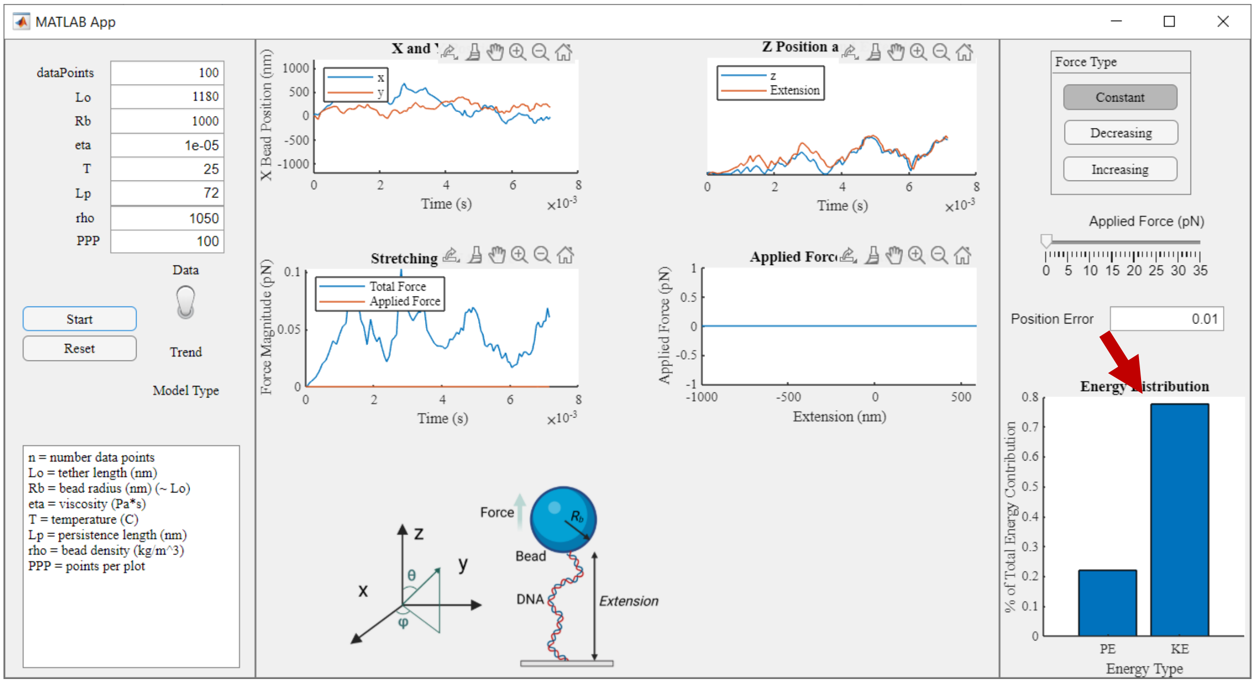

*Figure 11: Example of kinetic energy (KE) dominating. The viscosity (eta) was set to 10^{-5} Pa*s.*