Integration of Biological Observations and Theory into Computer Simulations of Bacterial Binding

Suron Woods

Bioengineering, Oregon State University

NNIN REU Site: Center for Nanotechnology, University of Washington, Seattle, WA

NNIN REU Principal Investigator: Wendy Thomas, Bioengineering, University of Washington

NNIN REU Mentor: Matt Whitfield, Bioengineering, University of Washington

Contact: suronwoods@gmail.com, wendyt@u.washington.edu, mjwhit16@u.washington.edu

Abstract:

Some biological adhesive bonds, called catch bonds, are enhanced by tensile force which enables complex behaviors at the cellular level. For example, *Escherichia coli* bacteria, binding to mannosylated surfaces via a catch-bond forming protein called FimH, switch from transient to rolling to stationary adhesion as hydrodynamic shear stress is increased, and detach again if the flow is turned off. The behavior of the catch bond is also influenced by the mechanical structure of the bacteria.

Our lab currently uses adhesive dynamic simulations and computational analysis to examine the relationship between catch bonds under shear stress, the mechanical structure of the fimbriae, and the behavior of the bacteria in fluid flow. The goal of this project is to design and implement into the simulation the additional functionality of fimbrial uncoiling so that the affect of this behavior on the catch bonds as well as the behavior of the bacteria can be determined via computational analysis. We created a two-state Monte Carlo algorithm using the polymer Worm-Like-Chain equation to model the behavior of the fimbriae under shear force.

Introduction:

The first step in successful colonization and infection of many bacteria is adhesion to host tissues. *Escherichia coli* adheres to mannosylated surfaces via a catch-bond forming protein called FimH, which is located at the tip of its fimbriae, which are long rods composed of more than 1000 coiled FimA protein subunits forming a helical structure anchored to the outer bacterial membrane. These fimbriae exhibit spring-like uncoiling behavior under shear force which mediate the forces at the FimH tip and enhances bacterial adhesion.

Mechanical measurements done on fimbriae using atomic force microscopes show that fimbriae readily extend under applied force, caused by the uncoiling of the FimA protein subunits [1]. This uncoiling produces a force plateau region in the force extension curve which is optimized to mediate the shear forces at the FimH tip and enhances the catch-bond lifetimes, which in turn enhances bacterial adhesion [2].

In order for our adhesive dynamic simulations to accurately model the behavior of bacterial in fluid flow, the uncoiling behavior of the fimbriae must be accurately modeled in our simulation. Once the modeling of fimbrial behavior is incorporated into the simulation, we can use the simulations to explore the dynamics of the FimH catch bonds and their role in the adhesion of bacteria.

Procedure:

The behavior of fimbriae under shear force has previously been probed in atomic force microscope (AFM) experiments. The data from these experiments has been used to determine the structure and behavior of fimbriae under force, which can be modeled using the polymer Worm-Like-Chain equation. These experiments also produced force extension curve data that we can use to compare with our simulation data to determine the accuracy of our simulation model, as seen in Figure 1.

We created a two-state Monte Carlo algorithm to model the uncoiling behavior of fimbriae, and incorporated this into our simulation of bacterial behavior in fluid flow. Previous experiments have shown this type of algorithm best models the uncoiling behavior of fimbriae [3].

Our simulation models the fimbriae much like a two spring force scenario. Using the overall fimbrial extension and the number of subunits in each state (coiled and uncoiled), we set the two force equations equal to each other and solved for the total tensile force from the fimbriae using an iterative method. The algorithm then used that force to calculate the uncoiling of the FimA subunits based on the probability of uncoiling adjacent subunits. These fimbrial forces were then used to determine the behavior of the FimH catch bonds, and summed to determine the overall behavior of the bacteria in fluid flow.

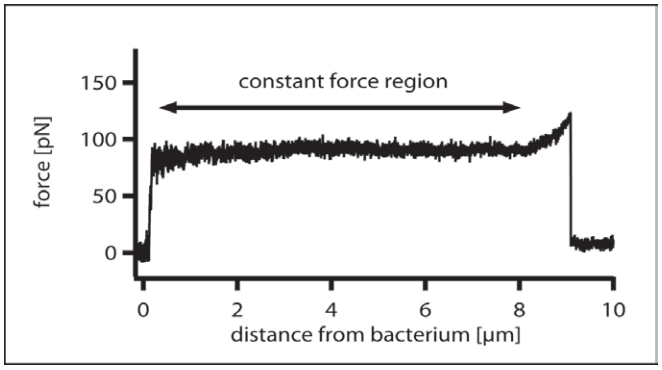

Figure 1: Force extension curve of uncoiling fimbriae from atomic force microscope experiments.

To determine the accuracy of our simulation, we ran the simulation using parameters to model a single fimbriae, and used the outputted simulation data to produce a force extension curve which we could compare to the data obtained from the AFM experiments.

Results and Conclusion:

Our simulation, resulting from modeling a single fimbriae, produced a force extension curve that matched the data obtained from AFM experiments. This was evidence that our simulation correctly modeled the behavior of single fimbriae under shear force. Thus, the simulation can be used to accurately describe and predict the behavior of bacteria in fluid flow, based on multiple fimbrial-surface interactions.

Future Work:

Our simulation can be used to run computational experiments to model the behavior of bacteria in fluid flow. Because these experiments are computational, we can alter parameters to explore the dynamics of fimbrial behavior, catch-bond interactions, and bacterial adhesion and behavior in fluid flow. In the future, this data may be used to fight bacterial disease or engineer adhesives that exhibit similar force dependant properties and behavior.

Acknowledgements:

I would like to thank the following for their assistance and support with this project: Wendy Thomas, Matt Whitfield, University of Washington Bioengineering Department, The National Nanotechnology Infrastructure Network Research Experience for Undergraduates Program, and The National Science Foundation.

References:

[1] Miller, Garcia, Hultgren, and Oberhauser. "The Mechanical Properties of E. coli Type 1 Pili Measured by Atomic Force Microscopy Techniques." Biophysical Journal 91 (2006): 3848-3856.

[2] Forero, Yakovenko, Sokurenko, Thomas, Vogel. "Uncoiling Mechanics of Escherichia coli Type I Fimbriae Are Optimized for Catch Bonds." PLOS Biology vol. 4 issue 9 e298 (2006): 1509-1516.

[3] Bjornham, Andersson. "Modeling of the elongation and retraction of Escherichia coli P pili under strain by Monte Carlo simulations." Eur. Biophysical Journal 37 (2008): 381-391.