

The mechanics of adhesion polymers and their role in bacterial attachment

Johan Zakrisson

Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för
avläggande av teknologie doktorsexamen framläggs till offentligt försvar
i N420, Naturvetarhuset
23:e oktober 2015, kl. 13:00.
Avhandlingen kommer att försvaras på engelska.

Fakultetsopponent: Professor, Kerstin Ramser,
Institutionen för teknikvetenskap och matematik, Luleå tekniska
universitet, Luleå, Sverige.



Department of physics
Umeå University
Umeå 2015

Organization
Umeå University
Department of physics

Document type
Doctoral thesis

Date of publication
30 September 2015

Author
Johan Zakrisson

Title
The mechanics of adhesion polymers and their role in bacterial attachment

Abstract

Bacterial resistance to antibiotics is increasing at a high rate in both developing and developed countries. To circumvent the problem of drug-resistant bacterial pathogens, we need to develop new effective methods, substances, and materials that can disarm and prevent them from causing infections. However, to do this we first need to find new possible targets in bacteria to approach and novel strategies to apply.

Escherichia coli (*E. coli*) bacteria is a normal member of the intestinal microflora of humans and mammals, but frequently cause diverse intestinal and external diseases by means of virulence factors, which leads to hundreds of million sick people each year with a high mortality rate. An *E. coli* bacterial infection starts with adhesion to a host cell using cell surface expressed adhesion polymers, called adhesion pili. Depending on the local environment different types of pili are expressed by the bacteria. For example, bacteria found in the gastrointestinal tract commonly express different pili in comparison to those found in the urinary tract and respiratory tract. These pili, which are vital for bacterial adhesion, thereby serve as a new possible approach in the fight against bacterial infections by targeting and disabling these structures using novel chemicals. However, in order to develop such chemicals, better understanding of these pili is needed.

Optical tweezers (OT) can measure and apply forces up to a few hundred pN with sub-pN force resolution and have shown to be an excellent tool for investigating mechanical properties of adhesion pili. It has been found that pili expressed by *E. coli* have a unique and complex force-extension response that is assumed to be important for the ability of bacteria to initiate and maintain attachment to the host cells. However, their mechanical functions and the advantage of specific mechanical functions, especially in the initial attachment process, have not yet been fully understood.

In this work, a detailed description of the pili mechanics and their role during cell adhesion is presented. By using results from optical tweezers force spectroscopy experiments in combination with physical modeling and numerical simulations, we investigated how pili can act as “shock absorbers” through uncoiling and thereby lower the fluid force acting on a bacterium. Our result demonstrate that the dynamic uncoiling capability of the helical part of the adhesion pili modulate the force to fit the optimal lifetime of its adhesin (the protein that binds to the receptor on the host cell), ensuring a high survival probability of the bond.

Since the attachment process is in proximity of a surface we also investigated the influence of tether properties and the importance of different surface corrections and additional force components to the Stokes drag force during simulations. The investigation showed that the surface corrections to the Stokes drag force and the Basset force cannot be neglected when simulating survival probability of a bond, since that can overestimate the probability by more than an order of magnitude.

Finally, a theoretical and experimental framework for two separate methods was developed. The first method can detect the presence of pili on single cells using optical tweezers. We verified the method using silica microspheres coated with a polymer brush and *E. coli* bacteria expressing; no pili, P pili, and type 1 pili, respectively. The second method was based on digital holography microscopy. Using the diffraction of semi-transparent object such as red blood cells, we showed that this method can reconstruct the axial position and detect morphological changes of cells.

Keywords

Optical tweezers, Pili, *Escherichia coli*, Force spectroscopy, Bacterial adhesion, Catch-bond, Fimbriae, Surface corrections, Digital holography

Language
English

ISBN
978-91-7601-331-1

Number of pages
77 + 7 papers