論文内容の要旨

論文題目　Bacterial flagellar filament protein unfolding/refolding mechanisms studied by molecular dynamics simulations
(分子動力学シミュレーションによる細菌べん毛繊維蛋白質のアンフォールディング)

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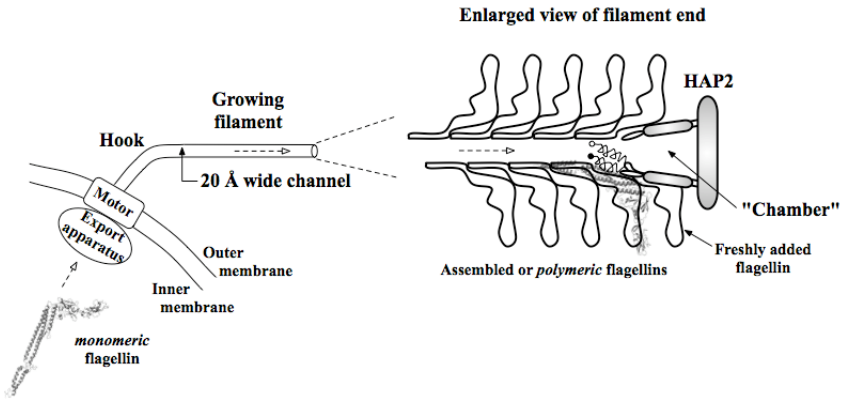
In the self-assembly process of the flagellar filament, the micrometer-long 'propeller' of the bacterial flagellum, subunit proteins called flagellin are polymerized into the growing filament. Flagellin from *S. typhimurium*, the only available flagellin structure at the time of this study, has two highly conserved helical filament-core domains (D0, D1) and two Hypervariable Region (HVR) domains (D2a/b, D3) rich in beta-strands that will be exposed on the filament surface in the assembled form. Flagellins synthesized in the bacterial cytoplasm have to travel through a channel in the center of the filament leading from the cytoplasm to a cavity or 'refolding chamber' under the filament cap. As the 20 Å diameter channel is too narrow for folded flagellin, this implies the coupling of unfolding/refolding processes to the protein transport. The study of these processes forms the focus of this thesis. It is known that cells contain machinery powered by ATP to unfold proteins by mechanical forces. The form flagellin takes during transport should be related to how it is unfolded. To investigate the preferred mechanical unfolding pathway of flagellin, force-probe molecular dynamics simulations have been used. Lower unfolding forces are associated with unraveling flagellin from its adjacently-located termini (producing a fully extended polypeptide chain) as compared to stretching flagellin along its length. After reaching the 'refolding chamber' at the distal end of the channel, flagellin has to be refolded before it can be assembled. Thermal unfolding simulations that probe spontaneous refolding suggest that persistent three-stranded beta-sheets in the denatured state of HVR domains might constitute folding initiation sites to guide refolding. Volume estimates indicated that the 'chamber' might accommodate only either denatured HVR domains or filament-core domains at any one time, suggesting a two-step refolding process with HVR domains folding and exiting the 'chamber' first.



Insights into this natural nanoscale transport system might form the basis for future bionanotechnology applications.