Exploring the biomechanics of type IV pilus filaments under force using coarse grained molecular dynamics

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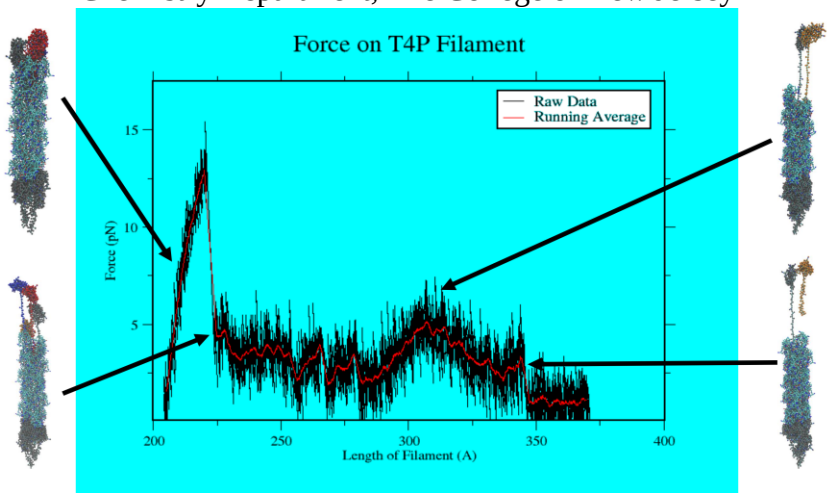

Type IV pili (T4P) are long biopolymers composed of many copies of a protein called pilin. T4P are both strong and flexible and are found on a wide variety of micro-organisms, including Gram-positive and Gram-negative bacteria, as well as archaea. In fact, it has been demonstrated experimentally that T4P can withstand extremely large tension forces (10,000 times the bacterial bodyweight), and under such force can go through an extensive conformational change in which they become three times longer and 40% narrower. Surprisingly, this transition was found to be fully reversible. However, a fundamental understanding of the great strength and flexibility of T4P are still not clear from the molecular perspective.

In this work, simulations of T4P filaments of *Neisseria gonorrhoea* (Ng T4P) and *Neisseria meningitidis* (Nm T4P) were carried out using a coarse grained model called the self-organized polymer (SOP) model. In the SOP model, interactions between coarse-grained beads are represented by finite extensible non-linear elastic potentials as well as attractive native contact interactions and repulsive non-native contact interactions between coarse-grained beads. We have created SOP coarse-grained models at both the alpha carbon level of resolution, as well as a level of resolution including one or two additional coarse-grained beads per amino acid, representing the side chain atoms.

While the SOP model is not suitable for probing the large-scale structural transition of the T4P filaments under force, it was used to obtain values of the T4P persistence length and its Young's modulus directly from the coarse-grained simulations. The Ng and Nm filaments were systematically stretched and bent to find the maximum force the filaments could withstand before losing structural integrity. Initial calculations of the T4P persistence length show that the calculated values fall within the experimentally measured persistence length values, and that the Young's modulus for the Nm T4P filament is comparatively lower than the Young's modulus for Ng T4P measured in a separate study. This is consistent with the results of force-extension experiments on these filament systems. In the future, we plan to more fully parameterize the interactions in the SOP model using all-atom data that we have for both the Ng T4P and Nm T4P filaments to determine if this improves our measurements of the T4P physical properties. Additionally, in order to measure the large scale extension of T4P under force, we will explore the use of coarse-grained models which are not native-contact based. Ultimately, understanding the fundamental mechanism at the molecular level of T4P stretching and bending will provide novel insights into potential applications of "T4P-like" biopolymers integrated in biological nano-devices.