Baseplate structure and its conformational changes required for genome delivery of *S. aureus* phage phi812

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Bacteriophage phi812 is a promising therapeutical agent for treating diseases caused by antimicrobial-resistant *Staphylococcus aureus*. In the initial stage of phage infection, phi812 uses a baseplate to recognize and attach to the host cell wall. The contractile tail of the phi812 acts as a nano-syringe that pierces the host cell to deliver the phage genome. To understand the molecular mechanism of phage infection, we reconstructed the tail and baseplate of phi812.

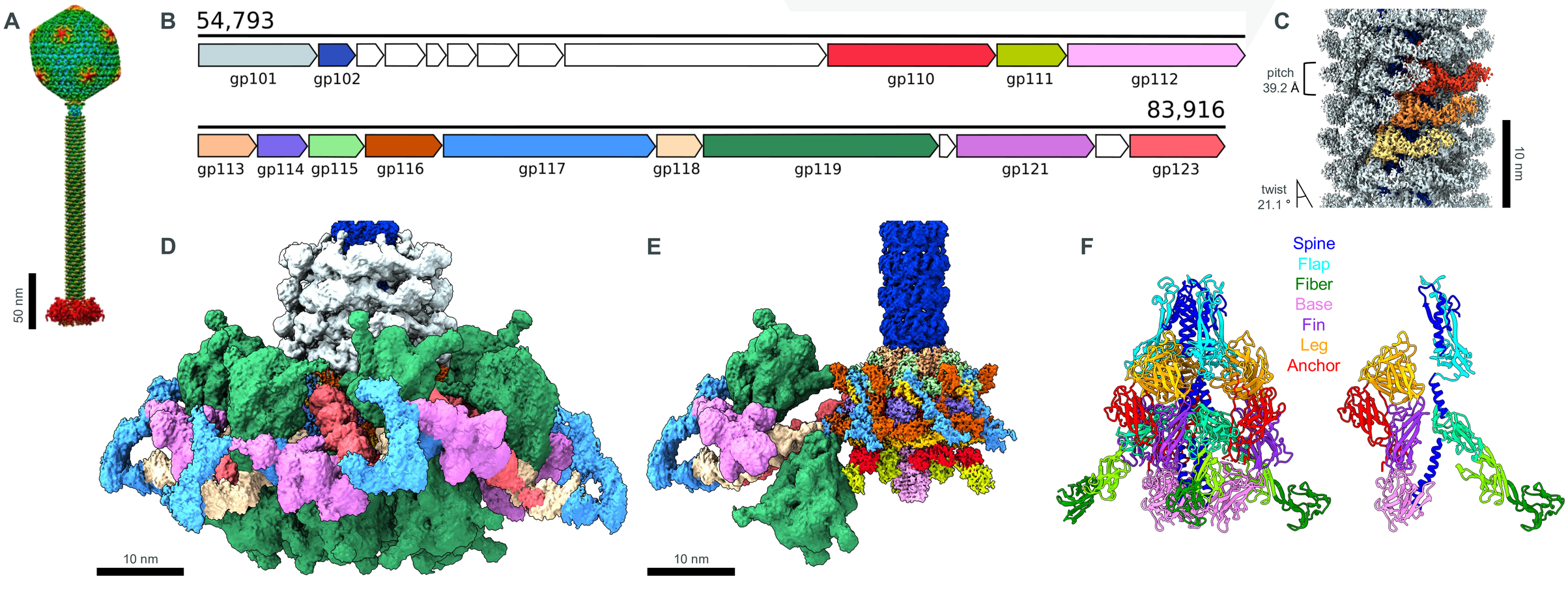

Figure 1: (A) Cryo-EM reconstruction of the phage phi812 in the pre-contraction state (adopted from Nováček, 2016). (B) Schematic representation of a segment of phi812 genome encoding structural proteins of the tail and baseplate. (C) Cryo-EM reconstruction of the pre-contraction tail. The tail sheath is colored grey except for the three sheath protein subunits of a single protofilament colored red, orange, and yellow. (D, E) Cryo-EM reconstruction of the pre-contraction baseplate shown with all six baseplate arms (D) and only one arm (E) to show proteins of the baseplate core. The densities are colored according to panel B. (F) Ribbon representation of the pre-contraction tripod protein (gp119) showed as a trimer (left) and monomer (right), colored according to its domains resolved in the reconstruction.

Upon interaction with the host cell wall, the baseplate undergoes structural re-organization. The cascade of positional and conformational changes propagate from outer baseplate proteins through the baseplate core to the tail, resulting in the contraction of the tail sheath. Tail sheath contraction drives the tail tube through the cell wall, which is degraded by phage enzymes found at the tip of the tail tube.

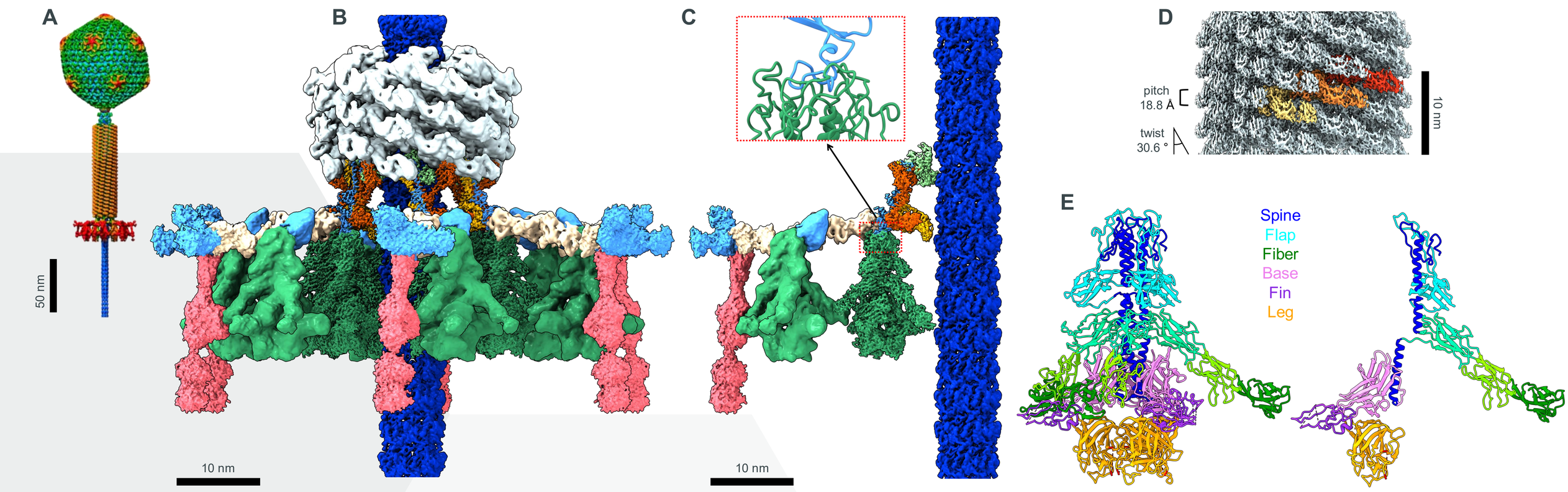

Figure 2: (A) Cryo-EM reconstruction of the phage phi812 in the post-contraction state (adopted from Nováček, 2016). (B, C) Cryo-EM reconstruction of the post-contraction baseplate shown with all six baseplate arms (B) and only one arm (C) to show proteins of the baseplate core. The inset in C shows an attachment of the trimer of tripod protein (gp119) to the arm scaffold protein (gp117), shown in the ribbon representation. The densities and ribbons are colored according to Fig. 1B. (D) Cryo-EM reconstruction of the post-contraction tail. The tail sheath is colored grey except for the three sheath protein subunits of a single protofilament colored red, orange, and yellow. (E) Ribbon representation of the post-contraction tripod protein (gp119) as a trimer (left) and monomer (right), colored according to its domains resolved in the reconstruction.

By comparing the two distinct baseplate states, we have described the initial stage of phage phi812 infection at the molecular level. Our study presents the first detailed structure of a phage with the contractile tail, which infects a Gram-positive bacterium. Thus, our findings provide a framework for engineering phage particles to combat *S. aureus* and other Gram-positive bacteria causing life-threatening infections in humans.

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