



Out of many, one, or a subunit assembly tale

Some of the most elegant and profitable adaptations of bacteria are, unfortunately, precisely what make these often-pathogenic organisms inimical to our own being. The long, filamentous pili projecting from the surface of many insidious bacterial pathogens (*Pseudomonas*, *Neisseria*, *Vibrio et al.*) represent one such adaptation. The type-IV pili considered here (there are several types) are required for host colonization and are used for several purposes, including adhesion to host cells. Because pili present such a conspicuous bacterial surface feature, they are also a convenient target of host defences, which of course, the pathogen would like to avoid. Shifting from the viewpoint of the microbiologist (or bacterium) to that of the structural biologist (or molecule), pili present another fascination—learning how the constituent pilin subunits assemble into the long, cable-like pili may reveal general principles involved in the assembly of analogous structures such as the well-studied actin filament, or other cytoskeletal filamentous multisubunit structures used for cellular function in eukaryotes.

Keeping in mind the various considerations above, the structure of a 17,400 M_r pilin from *N. gonorrhoeae* (H.E. Parge *et al.* *Nature* **378**, 32–38, 1995) is a satisfying advance. Fibre-forming proteins are difficult to crystallize due to their propensity for self-assembly; crystallization of pilin was achieved by stabilizing a dimeric form. Knowledge of the subunit structure has allowed construction of a model of the pilin fibre shown at left (top: end view; bottom: longitudinal view). An individual 85 Å-long pilin subunit (consider the lighter yellow subunit in the longitudinal view) is shaped like a ladle. The N-terminal handle is an α -helix that runs the length of the monomer, describing a gentle s-shaped curve—only the most N-terminal half of the helix can be seen descending from the ladle head, whose convex back is turned toward the outside of the fibre model. The head region is composed primarily of six β -strands and includes a C-terminal disulphide-linked tail and a covalently linked disaccharide (white), exposed on the back surface of the ladle. Parge *et al.* propose the multisubunit fibre model shown based on previous fibre diffraction measurements of type-IV pili from *P. aeruginosa* (another model, based on tail-to-tail subunit associations, while formally possible, does not fit the fibre diffraction data). In the model, five subunits (green, magenta, red, yellow, blue) complete a turn in a continuous spiral, packing with the flat side of their head regions facing inward against the handles of subunits from successive turns (denoted in muted and bright colours). The subunit handles on the inside of the fibre are associated in a parallel coiled-coil (at bottom of longitudinal view).

As mentioned above, pili are the target of host antibodies. To frustrate an immune response, the head domain of pilin has a variable sequence, particularly within the disulphide domain. In this model this domain is on the outside of the fibre, exposed to a potential host attack, while the invariant parts of the structure—constrained from sequence variance because they are required for subunit assembly—remain on the inside. The exposed saccharides could modulate specificity of binding to host cells.

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