

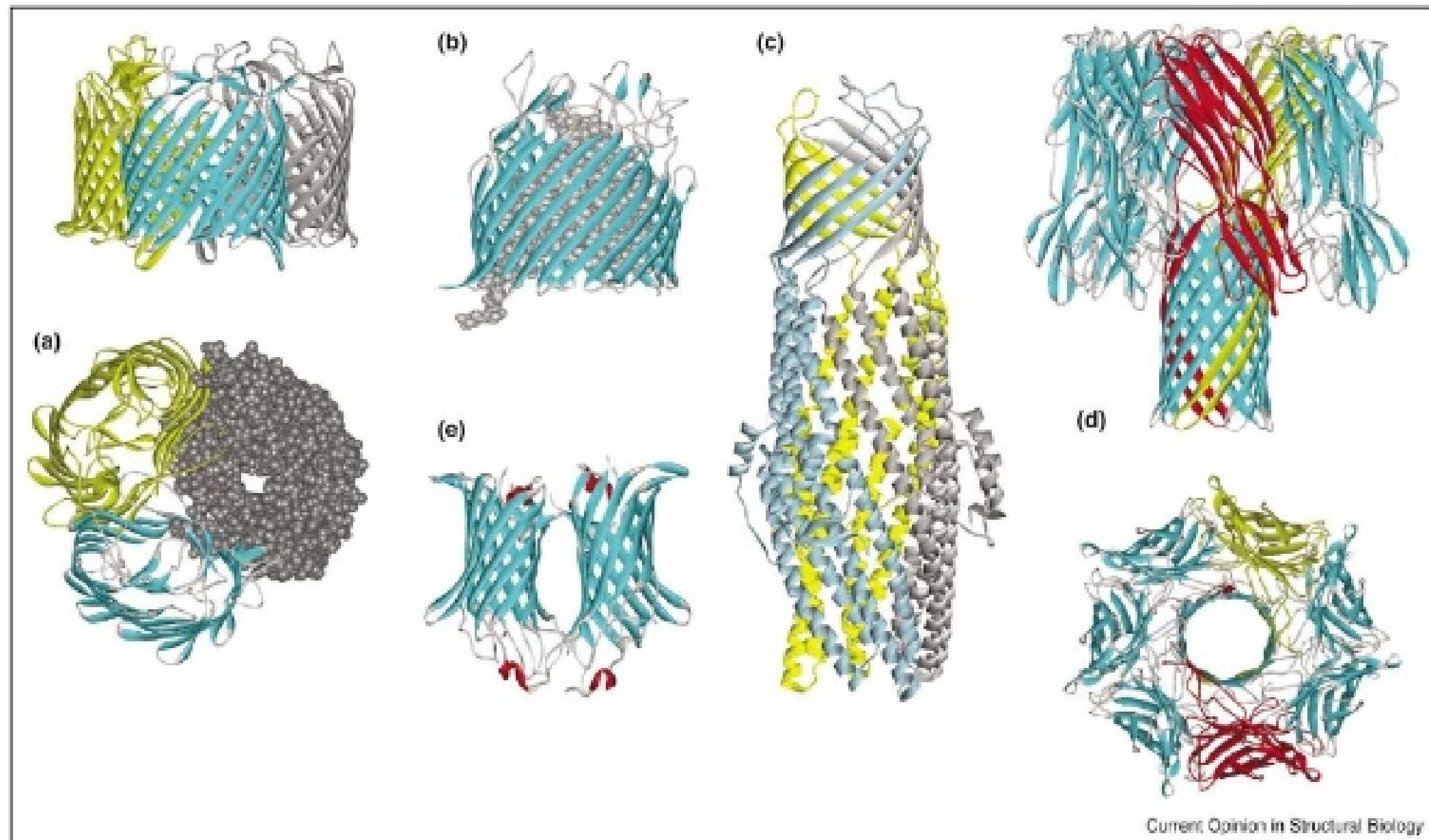
Architecture of a β -barrel membrane protein. **(a)** Exposed and buried residues of the *E. coli* β -barrel protein OmpX. Residues in the membrane-spanning part of this eight-stranded β -barrel are either red (lipid exposed) or black (barrel interior). Extramembranous loops are green. The y-axis shows the protein's dimensions across the membrane in angstroms, with the origin at the bilayer mid-plane [11**]. The horizontal lines at 13.5 Å denote the limits of the hydrophobic part of the membrane [11**]. The network of hydrogen bonds that stabilizes the barrel in the membrane is also shown by black lines. Each hydrogen bond can contribute as much as 0.5 kcal/mol/residue to stability, as suggested by peptide studies [3,6,7]. Thus, hydrogen bonding can easily account for the high stability of β -barrel membrane proteins. The eighth, C-terminal TM β -strand is repeated in gray at the far left. **(b)** Structure of OmpX. The side view shows the β -strands on the same y-scale as in (a), with the membrane-spanning strands in gray. Notice the abundance of aromatic residues on the lipid-exposed surface, in yellow. The bottom view shows the disposition of the sidechains in the barrel using the same color scheme as in (a): red, lipid exposed; black, barrel interior. Extramembranous loops are not shown. **(c,d)** Abundance of amino acids in β -barrels compared to the overall genomic abundance [11**]. External surfaces (c) are dominated by aromatic residues, whereas internal residues (d) are dominated by small and polar amino acids.

Table 1

A variety of functions that are provided by β -barrel membrane proteins*.

| Functional category | One example | Structure (PDB accession) |
|-------------------------------------|---------------------|---------------------------|
| Nonspecific porin | OmpF | 2OMF |
| Facilitated transporter | Maltoporin | 1MPR |
| Energy-dependent transporter-efflux | ToIC | 1QJ8 |
| Energy-dependent transporter-influx | FepA | 1FEP |
| Protein secretion pore | PuID | NA |
| OM usher pore | PapC | NA |
| Adhesin | OmpX | 1QJ8 |
| Lipase | OmpLA | 1QD6 |
| Protease | OmpT | 1I78 |
| Mitochondria protein import pore | Tom40 | NA |
| Protein pore-forming toxin | α -Hemolysin | 7AHL |

*For each category, I give one example for which some detailed information is known. These are broad functional categories. Some of them include multiple distinct families of proteins with hundreds of known members [25**]. A PDB accession number is given for those examples for which a three-dimensional structure is known. NA, not available.



A gallery of β -barrel membrane protein structures. **(a)** Maltoporin, side view (upper) and bottom view (lower). Maltoporin is an example of the trimeric β -barrel porins, which are either nonspecific or facilitated transporters in the OM of Gram-negative bacteria [51]. Maltoporin is a maltose transporter. Known trimeric porins have 16 or 18 TM strands, which comprise three separate barrels in the trimer. Each of the barrels contains a narrow, central channel. **(b)** FepA, a TonB-dependent Fe-siderophore transporter [52]. The four TonB-dependent receptors of known structure all have 22 membrane-spanning β -strands comprising a C-terminal β -barrel domain. They also have an N-terminal 'hatch' domain, shown here in gray space-filling representation, that plugs the barrel and regulates transport. TonB-dependent transporters use metabolic energy through interactions with inner membrane proteins [52,53]. **(c)** The protein TolC is a small-molecule exporter belonging to the OM factor family [25^{***},54]. TolC is involved in multidrug resistance of bacteria. It derives metabolic energy from its interaction with the inner bacterial membrane. TolC is unique among known β -barrel structures, comprising a trimeric, 12-stranded single barrel [55] in which each monomer contributes four strands to the barrel. The pore of the β -barrel is connected to the pore of a hollow α -helical bundle that extends across the periplasmic space to the inner membrane. **(d)** The protein toxin α -hemolysin from *S. aureus* [22,49]. This toxin is secreted as a monomeric protein that subsequently assembles into a heptameric 'prepore' on the membrane, followed by the cooperative insertion of the β -barrel across the membrane. Each monomer contributes one β -hairpin to the 14-stranded barrel. The central pore is an ungated path through the membrane that leads to osmotic cytolysis. The upper image is a side view and the lower image is a bottom view of the heptameric pore. **(e)** OmpLA, an OM phospholipase [56]. OmpLA is a dimer of 12-stranded barrels. The role of OmpLA may be to hydrolyze phospholipids that have migrated to the outer surface of the OM, where they are normally not present [56].