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Brice Barbat, Badreddine Douzi, Romé Voulhoux

STRUCTURAL LESSONS ON BACTERIAL SECRETINS

Brice Barbat[1], Badreddine Douzi[2] & Romé Voulhoux[1]*

[1]LCB-UMR7283, CNRS, Aix Marseille Université, IMM, 13009 Marseille, France
[2]Université de Lorraine, INRAE, DynAMic, 54000 Nancy, France

***Correspondance :**
Email : voulhoux@imm.cnrs.fr
Postal address : LCB-UMR7283, CNRS, Aix Marseille Université, IMM, 31 Ch. J. Aiguier 13009 Marseille, France

ABSTRACT

To exchange and communicate with their surroundings, bacteria have evolved multiple active and passive mechanisms for trans-envelope transport. Among the pore-forming complexes found in the outer membrane of Gram-negative bacteria, secretins are distinctive homo-oligomeric channels dedicated to the active translocation of voluminous structures such as folded proteins, assembled fibers, virus particles or DNA. Members of the bacterial secretin family share a common cylinder-shaped structure with a gated pore-forming part inserted in the outer membrane, and a periplasmic channel connected to the inner membrane components of the corresponding nanomachine. In this mini-review, we will present what recently determined 3D structures have told us about the mechanisms of translocation through secretins of large substrates to the bacterial surface or in the extracellular milieu.

KEYWORDS

bacterial secretin; beta-barrel; outer membrane; cryo-EM; structure-function

HIGHLIGHTS

- Secretins are the OM portal of the T2SS, T3SS, T4P and FPE systems
- Secretins form giant pores tailored to the secretion or assembly of large structures
- Secretins consist of a conserved OM C-module and a variable periplasmic N-module
- The channel formed by the C-module is occluded by a flexible central gate (CG)
- The N-module connect with the IM components of the respective systems

1. Introduction

Secretins were discovered in the 80's during the study of *Klebsiella oxytoca* outer membrane (OM) constituents responsible for the export of folded pullulanase to the extracellular milieu [1]. Secretins have been intensively since because of their unique ability to accommodate large folded exoproteins and protein complexes in several bacterial transport nanomachines [2]. Due to their function, secretins were thought for decades to form giant ring-shaped homo-oligomers in the OM [3-8], but their precise atomic organization was deciphered only recently thanks to spectacular advances in cryo-electron microscopy (cryo-EM) [9, 10]. This revealed extraordinary ternary and quaternary networks, highlighting unsuspected structural determinants at the basis of functions hitherto observed but not yet understood. In this mini-review, we will present how cryo-EM structural data shed light on the architecture and function of bacterial secretins, and how structural determinants compartmentalize and animate these giant pores embedded in the bacterial envelope.

2. The bacterial secretin family

The existence of a bacterial secretin family, first proposed by Genin and colleagues, comprised several OM-associated proteins essential for the transport of macromolecules across bacterial membranes [11]. Bacterial secretins are widely used by bacteria and even by mitochondria [12] in a variety of transport systems specialized in the transit of large molecules across the OM. These range from delivery of folded effectors by the Type 2 Secretion System (T2SS) to filament accommodation in the case of the Type 3 Secretion System (T3SS) and Type 4 Pili (T4P) or phage release in the Filamentous Phage Extrusion (FPE) system. Members of this family were historically defined by a highly conserved C-terminal "secretin domain" which appeared to be the OM pore-forming domain [13], and a variety of N-terminal domains, combinations of distinct modular domains connected via short linkers, whose number depends on the transport machine [14]. For example, while the T2SS-secretin N-part is composed of three repeated N3, N2 and N1 Ring-Building Motif (RBM) domains and a N0 TonB-dependent transduction domain [15] possibly supplemented by a peptidoglycan binding SPOR domain [16], the N-part of the other secretin types (T4P and FPE) are made up of N3 and N0 domains, optionally completed by an internal N1 sub-domain for T3SS or two distal amidase N-terminal "AMIN" domains for T4P [17]. Finally, the T2SS and T3SS secretins possess an additional extreme C-terminal S-domain, the attachment site for a partner protein called pilotin, which assists secretin assembly and targeting to the OM (see [18] for review).

3. Cryo-EM reveals atomic 3D architecture of secretins

3.1 Overall organization

Recent advances in the field of cryo-EM applied to isolated biological samples led to high-resolution 3D structures for at least one member of each bacterial secretin type (see Table 1 for an exhaustive list of secretin near-atomic-resolution cryo-EM structures available). These structures – illustrative examples are presented Figure 1 – revealed a bimodular organization with a well-defined OM C-module, followed by a periplasmic variable N-module composed of several superposed ring-like structures connected by short linkers. In most secretin structures, the C-module is resolved at a resolution of 3-4 Å, whereas the resolution decreases over the N-module to become poor in the most N-terminal N0 domain. It has been hypothesized that this results from the N0 domain high flexibility in absence of its inner membrane (IM) interacting partner. This is in line with N0 high resolution in the structure of the T2SS PulD secretin of *Klebsiella pneumoniae* copurified with its IM partner PulC [19]. The C-module found in all secretins has a structural organization into three domains, which could not

be predicted from the primary sequence. First, there is a giant double wall β-barrel with a closed central gate (CG) that must open to allow the passage of the translocated structures. In some T2SS secretins, the channel is capped by an additional top gate (TG). Second, we consider the N3 RBM-domain, originally thought to be part of the N-domain, as part of the pore-forming C-module, which is consistent with its structural role and conservation in secretins [20]. Finally, the extreme C-terminal S-domain (specific of T2SS and T3SS-secretins) is composed of 2 α-helices that encircled the outer barrel.

3.2. Stoichiometry

The exact stoichiometry of secretins has always been and still is a matter of debate. Previous low-resolution 3D structures suggested a homo-multimeric organization of 12, 14 or 15 subunits depending on the type [14]. The recently reported high-resolution structures (listed in Table 1) are compatible with these stoichiometries, at least for the C-modules. Either isolated or in complexes, T2SS, T3SS and FPE secretins C-modules present a definite pentadecameric (C15) symmetry, whereas T4P secretins primarily adopt a tetradecameric (C14) symmetry. Interestingly, different stoichiometries have sometimes been reported for a given secretin C-module, e.g., 28 % of the *Escherichia coli* T2SS GspD are hexadecameric (C16) [10], while 8 % of the *Pseudomonas aeruginosa* T4P PilQ adopt a C15 symmetry [21]. This variability does not appear to be restricted to secretin types, and it could therefore constitute an additional adaptation to accommodate complex secretion/assembly processes.

The stoichiometry of N-modules is less well understood since their 3D structures are poorly, or not at all, resolved, probably due to high intrinsic flexibility. This is regrettable because there is a recurrent symmetry conflict for T3SS and T2SS secretins between C-modules and IM partners, which present incompatible 15:24 and 15:12 stoichiometries, respectively [19, 22]. Recently, structures of T3SS complexes including secretins and their IM partners indicate that the stoichiometry mismatch could be resolved by the presence of additional secretin domains. In the case of *Salmonella enterica* serovar Typhimurium T3SS, the presence of a sixteenth secretin subunit is clearly seen for the N0-N1 domains, leading to a compatible $InvG_{16}$:$PrgH_{24}$ interface with 8 additional PrgH subunits packing around and under the β-sheet to reinforce the interface [22]. The addition of N0-N1 monomers in a pentadecameric secretin was also observed for the *Shigella flexneri* T3SS secretin MxiD [23, 24]. For T2SS, the interface region between the PulD N0 domain and its IM partner PulC is also puzzling with an estimation of around 15 PulD-N0 for about 12 PulC-HR, leaving up to three PulD-N0 unoccupied [19]. Independent work showed that the *P. aeruginosa* T2SS secretin XcpD (formerly XcpQ) adopts a dodecameric (C12) conformation when purified without the C-module [25]. As proposed by Hay and colleagues [26], such symmetry mismatch in T2SS secretins might be overcome by the displacement of three XcpD N-modules away from the XcpC IM-partner-interface, thus leading to the formation of the metastable C15:N12 arrangement. The overall stoichiometry of a given secretin might therefore fluctuate, especially in its N-terminal part, to be compatible with the stoichiometry of its IM partner. However, additional structural data is needed for a more complete understanding of this conundrum.

3.3. Charge distributions

While their structures are similar, the internal electrostatic characteristics of bacterial secretins vary significantly from one secretin type to another but also within the same type (figure 2) [27, 28, 30]. The overall amount of charged amino acids is around 20 % depending on the secretin's type, but their distribution on the quaternary structure is not homogeneous along the channel of each secretin. On the structures available to date, it seems that the entry of the internal cavity in the N-terminal side has a relatively positive charge, whereas in the N3 domain it turns to be relatively negative except for FPE

secretins. An important charge heterogeneity is found in a disordered loop in the N3-domain of variable size, but neither its structural importance nor its functional role have been determined yet. The variation of charge in the lower cavity could be important to stabilize the assembled filament inside the secretin, or to allow the docking of the folded effector in T2SS, but these hypotheses have never been investigated. Looking at the CG of T3SS secretins, we observe a predominant charge that is opposite to the charge present on the wall of the upper cavity. Such charge distribution could allow stabilization of the central gate once it is open considering that it stays open in this secretin when the needle is assembled. The charge compatibility between the top of the CG and the β-barrel wall is not seen in the T2SS, T4P and FPE secretins where these regions display relatively similar charge distributions. In terms of dynamics, the presence of identical charges in these zones would lead to electrostatic repulsion and therefore could allow rapid closing of the CG when the pseudopilus or pilus is disassembled in the T2SS and T4P systems or when the phage particle has been secreted in the FPE system. If we compare the different secretin types, the apical extremities show a wide range of global charges (compare for example T4P and FPE secretins in figure 2), which could be an evolutionary adaptation to their external environment.

4. Secretin structures reveal discrete common and specific features

4.1. The gated pore-forming domain

The pore-forming domain of bacterial secretins is highly conserved and form the OM portal through which secreted substrates or translocated appendages transit to the cell surface. Recent cryo-EM data revealed an atypical organization into a giant 56 to 64 stranded β-barrel, where each of the 14-16 subunits contributing a 4-stranded beta sheet (Table 1 and Figure 1). The high-resolution structures also revealed an additional inner barrel formed by 4 β-strand per monomers, with the two upper strands extending towards the center of the cavity, perpendicularly to the barrel wall, a structural feature already suspected in many low-resolution structures of secretins [8, 20, 31]. The convergence of their loops in the center of the cavity partially obturates the channel to form an orifice of variable size, depending on the secretin type, but always too narrow to allow the transit of its corresponding molecule. This observation agrees with previous studies of secretin channels pore size and electrophysiology showing a pore with a small opening, akin to regular porins [7, 13, 32, 33]. This structural feature separates the periplasmic chamber from the top cavity and is therefore named central gate (CG) (Figure 1). The gating function of CG is supported by the fact that most of the previously identified mutations in the FPE F1 phage secretin pIV, leading to gain of function growth on maltopentaose, bile salt permeability or antibiotic sensibility [34], mapped to the CG [27]. CGs, most often captured under closed conformation in isolated particles, must adopt an alternative open conformation to allow the passage of the different structures secreted or assembled by secretins. Such flexibility is comforted by the observation of a partially open CG and bile salt-sensitive phenotype for the T2SS $GspD_{G453A}$ variant, which harbors a glycine to alanine substitution in the central gate [10]. Sequence alignment of secretins show that glycine residues are systematically present at least at one bending point of the CG β-strands. In accord with their high flexibility, these residues would allow the rotation of the CG, which would flip upwards and come close to the β-barrel wall to accommodate the secreted or assembled structure. Such opening mechanism has recently been confirmed by the 3D structure of the T3SS secretin InvG in an open conformation with the needle assembled inside (Figure 1) [22]. Importantly, since CG modification not only results in leaky but also non-functional secretins, passage through the CG is probably not a passive process [34]. Given the structural and functional diversity of the molecules passing through this channel, it is not surprising that this diversity is reflected

in the CG primary sequences. It is indeed easy to imagine that to accommodate a static needle (T3SS), a folded effector (T2SS), a highly dynamic pilus (T4P) or a bacteriophage (FPE), bacterial secretins must display different CGs composition and dynamics. Interestingly, even among T2SS secretins, significant sequence divergence exists in CGs that may reflect the exquisite substrate specificity existing between different T2SS [10]. However, we still lack biochemical data on the interaction interfaces between CGs and substrates to understand mechanistically how CGs function in different types of secretins.

4.2. The N3 RBM domain and its involvement in pore formation

Global observation of secretin 3D structures (Figure 1) indicates that the N3 domain, previously associated by sequence homology to the periplasmic N-domains, constitutes the building blocks of the C-module with the pore-forming domain. This structural reallocation of the N3 domain to the C-module confirms previous functional data showing its requirement, in addition to the pore-forming domain, for the assembly of a minimal secretin capable of forming a pore in the OM [13, 35]. The N3 RBM domain has the propensity to form ring-like structures [36]. RBMs are also found outside of bacterial secretins where they also play a central ring-building function, e.g., in the IM ring of the T3SS [37] or the sporulation channel component SpoIIIAG [38]. Since T2SS secretins are independent of the β-barrel assembly machinery (BAM), pre-folded in the periplasm and able to fold spontaneously *in vitro* [39], it is tempting to speculate that the circular oligomerization of secretin C-module could be driven by the ring-like self-assembly property of their RBM domain [37]. This notion is however challenged by a recent structural study indicating that RBM most likely stabilise the oligomer rather than initiate its oligomerization [40]. Nonetheless, RBM conservation in all secretins, as well as its essentiality for oligomerization, support its reallocation as part of the upper C-module.

4.3. Secretin biogenesis and its scaffolding S domain

The different steps driving a protein initially synthesized in the cytoplasm to its final conformation and location consist in overcoming multiple constraints. The secretins must not only travel to the OM but also adopt a complex channel conformation, allowing the passage of large molecules without perturbing bacterial envelope integrity. Their final destination being beyond the IM, the newly synthetized pro-secretin monomer is taken over in the cytoplasm by the SecB chaperone to be exported in the periplasm through the Sec translocon. Once exported, and after cleavage of the signal sequence, secretin monomers are, most often, taken over by an escort protein called pilotin, which will assist in their delivery and proper insertion into the OM [41]. Pilotin maintains the secretin in an intermediate conformation compatible with its transport to the OM, preventing mis-localization and/or premature oligomerization in the IM, which would be deleterious to cell integrity. Such phenotypes have indeed been observed for T2SS and T3SS secretins in absence of their pilotins [42, 43]. Several types of mechanisms have been described for the transport of secretins from the periplasm to the outer membrane [44]. The most common, used by most T2SS and T3SS secretins, involves a lipidated pilotin, itself transported to the OM via the Lol pathway [45]. In this case, secretin transport to the OM is independent of the BAM pathway [46] in agreement with its non-β-barreled OM inserted domain [28] and its capacity to spontaneously insert in artificial vesicles [35]. Alternative OM targeting for secretins have been described including Bam-dependent transport [47], involvement of IM accessory proteins for T4P and T2SS secretins [41, 48], or no external assistance like for the self-piloted T2SS HxcQ lipo-secretin [49]. Regarding secretin assembly, the existence of folded periplasmic intermediates adopting different conformations prior to the OM insertion has been proposed [39].

Such process has been observed in many pore-forming proteins [50-52] and also supported by the capacity of secretins to oligomerize outside the OM.

T2SS and T3SS secretins localization, assembly and OM insertion are mostly governed by their extreme C-terminal S-domains reviewed by [53]. In the high-resolution structures, these S-domains form a helix-turn-helix motif that extends laterally on the exterior of the β-barrel (Figure 1). This supports the notion that S-domains have a key role in efficient secretin assembly and stability in addition to their pilotin-binding function. S-domains are necessary and sufficient to ensure targeting and stabilization since the graft of the PulD or InvG S-domains to the S-domain deficient FPE pIV secretin rendered the chimeras functional, dependent on the PulS and InvH pilotins, respectively [54, 55]. S-domains of T2SS pilotin-dependent secretins are formed by 2 α-helices, respectively involved in stabilization and pilotin recognition. This structure-function relationship is confirmed by the absence of the second helix in secretins targeting to the OM by an alternative pilotin-independent process [48], or for which no pilotin has yet been identified. This is the case for XcpD of *P. aeruginosa* [26] for which, another mode of OM targeting could be considered.

4.4. The periplasmic N-module composed of several successive N-domains

With the N3 RBM domain now considered part of the C-module, the secretin N-module is therefore defined as the portion comprising all the domains N-terminal to the N3 RBM domain (Figure 1). Unlike the C-module whose high-resolution structure allowed the precise positioning of each monomer up to amino acids side chains, the lower resolution of N-modules does not allow a clear identification of the monomers. In the majority of the available structures, the N-domains were only positioned by homology-based building using monomeric crystal structures, thus often leading to steric clashes and therefore questioning the accuracy of the models [9, 10, 26, 27, 30]. Such low resolution of N-modules was systematically seen with the first isolated secretin structures, suggesting the requirement of stabilizing partners, which was confirmed subsequently for complexes between secretins and their IM partners [19, 56]. These structures indicate that the N-module is clearly dissociated from the C-module through an unstructured density (Figure 1). This poorly resolved flexible zone may correspond to the inter-domain region separating the OM-associated C-module and the periplasmic N-module. The flexibility in the inter-domain region could allow for important structural rearrangements, essential for the coexistence of the previously discussed different structural organization and stoichiometry between the C- and N-modules.

All bacterial secretins harbour a N0 domain at their extreme N-terminus, which is involved in IM-coupling. While N0 structure was not resolved in secretin oligomers, it has been determined for monomeric truncated variants or oligomers in complex with their IM partners [22, 25, 27, 30, 57, 58]. N0 domains of T2SS, T4P, FPE and to some extent T3SS secretins have a similar structural organization, thus suggesting a conserved packing arrangement among secretins. At the quaternary level, structures obtained in combination with IM partners show that the N0 is oriented perpendicularly to the N-domain above it (N1 for T2SS/T3SS, and N3 for T4P) [19, 56], while it is positioned in a parallel fashion in absence of IM partners (Figure 1) [25, 58, 59]. N0 domains organization within secretin channels appears to be highly variable even in term of stoichiometry. Inside a specific secretin family such as T3SS, pentadecameric and hexadecameric organization have been proposed [22, 56]. For T2SS, pentadecamers and dodecamers (hexamers of dimers), both physiologically relevant, were reported [19, 25].

In addition to the conserved N0 domain, additional RBM domains are sometimes found between N3 and N0. This is the case for T2SS and T3SS secretins N-modules, which display two RBMs (N1 and

N2) and one RBM (N1), respectively. These domains could define the size of the periplasmic chamber therefore reflecting the nature of the envelope in which they are inserted. For example, in the thermophilic bacterium *Thermus thermophilus*, the T4P secretin PilQ has an N-module composed of five stacked rings, including four RBMs all dispensable for complex assembly but essential for function [60]. This larger N-module could represent an adaptation to the thicker cell envelope of this bacterium.

4.5. Discovery of an optional top-gate (TG) in a sub-class of secretins

As new secretin structures were released (Table 1), common and specific determinants of the different family members have emerged. This was the case for T2SS secretins, for which several structures revealed the existence in the *Vibrio*-type subclass [61] of an additional apical domain called top-gate (TG) or cap-gate (Figure 1) [10]. The TG has a conical structure formed by the convergence of 15 pairs of antiparallel β-strands whose connecting loops are relatively loose, suggesting that the hairpin formed by the TG is a dynamic structure alike the CG. The inner diameter of the TG defines a much narrower opening compared to the large open-edged β-barrels formed by the other subclass lacking TG and called *Klebsiella*-type (Figure 1). Given the directionality of effector transport in T2SS, the TG should rotate outward to open and release the substrate in the extracellular medium. After substrate release, the TG would return to its closed conformation to eventually start a new cycle. The presence of such a structure at the top of some T2SS secretins could represent an additional gasket preventing the entry of toxic molecules. Until now, no other type of secretins displayed obvious TG at their summit (Figure 1 and Table 1), an observation consistent with the absence of a corresponding region in their primary sequences [9].

5. Concluding remarks

Structural and functional study of bacterial secretins, which remained a mystery for more than 30 years, has largely benefited from the spectacular advances in structural biology and notably from the breakthrough of cryo-EM. This revealed intriguing and sometimes unexpected quaternary features of these giant gated double-barrelled channels – such as the interlacement and intertwining of unrelated secondary and ternary structures of each monomer in gates, barrels or cages – providing a coherent atomic quaternary picture. As we move towards a better mechanistic understanding of bacterial secretins, several important challenges remain, including how secretins are transported, assembled and inserted in the OM, how they open and close without compromising their remarkable stability. We need to understand how these giant pores are motioned in the global secretion/assembly context of their corresponding nanomachines, particularly for their poorly resolved N-terminal regions. The ultimate goal – visualizing, at atomic scale, the secretins in their natural environment the bacterial envelope – awaits a revolution in cryo-electron tomography allowing atomic resolution to be reached.

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Conflict of interest.

None

Contributions

B. Barbat, B. Douzi and R. Voulhoux contributed to the design and the writing of the manuscript, B. Barbat designed the figures and R. Voulhoux supervised the work.

Figures & Table legends

Figure 1. Representative cryo-EM structures for each secretin type. The PDB structures have been scaled, aligned with the outer membrane (shaded orange rectangle), and colored according to the following code. Red, monomer; gray, C-module (C+N3 domains); blue, N-module (N0±N1±N2 domains); green, S-domain; pink, PulS pilotin; orange, PulC IM-partner. (**Top**) Side view. The missing N0 domain is represented by a shaded blue cylinder. The two different *Vibrio* (*V*) and *Klebsiella* (*K*) types of T2SS secretins [61] are presented, as well as the "closed" (C) and "open" (O) states of the InvG T3SS secretin. (**Bottom**) Cross-section view highlighting top-gate (TG) and central-gate (CG) constrictions, as well as internal diameters. The disordered loops in N3 domains are indicated by *. Dimensions (in Å) are from measurements on the PDB entries.

Figure 2. Charge distribution of internal cavities in different secretin types. The vertical cross-section of the secretins presented in Figure 1, colored according to their inner surface charge using the APBS Electrostatics Plug-in available in PyMol [29]. The color r scale is shown on the left. The position of N3 domains is indicated by a grey bar.

Table 1. List of cryo-EM 3D structures of bacterial secretins at near-atomic resolution. Secretins for which a near-atomic resolution structure (<7Å) has been published is listed. For each structure, the name of the secretin and its organism of origin, its PDB entry, the stoichiometry, domains that are resolved and the overall resolution are indicated. When useful, additional information on specific features of the structure is provided.

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System	PDB entry	Secretin name	Organism	Domains	Resolution	Secretin's Stoichiometry	Remarks (in complex with)	Reference
T2SS	5WLN	XcpD	*P. aeruginosa*	*S/C/N3/N2*	*3.57* Å	*15*		[26]
	6I1X	ExeD	*A. hydrophila*	*S/C/N3/N2/N1*	*3.7* Å	*15*		[48]
	5W68	GspD	*E. coli EPEC*	*S/C/N3*	*3.3* Å	*15*	Top Gate	[28]
	5ZDH	GspD	*E. coli ETEC*	*S/C/N3/N2/N1*	*3.2* Å	*15*	Top Gate (AspS)	[62]
	5WQ7	GspD	*E. coli K12*	*S/C/N3/N2/N1*	*3.04* Å	*15 & 16*		[10]
	5WQ8	GspD	*V. cholerae*	*S/C/N3/N2/N1*	*3.26* Å	*15*	Top Gate	[10]
	5WQ9	$GspD_{G453A}$	*V. cholerae*	*S/C/N3/N2/N1*	*4.22* Å	*15*	Partially open state	[10]
	6I1Y	EpsD	*V. vulnificus*	*S/C/N3/N2/N1*	*3.4* Å	*15*	Top gate	[48]
	6HCG	PulD	*K. pneumoniae*	*S/C/N3/N2/N1/N0*	*4.3* Å	*15*	(PulCS)	[19]
T3SS	6DV3	InvG	*S. enterica*	*S/C/N3/N1/N0*	*4.1* Å	*15*	Open state	[22]
	6DV6	InvG	*S. enterica*	*S/C/N3*	*3.9* Å	*15*	Open state	[22]
	6PEE	InvG	*S. enterica*	*S/C/N3*	*3.42* Å	*15*		[56]
	6PEP	InvG	*S. enterica*	*N1/N0*	*3.8* Å	*16*	(SpaPQR:PrgHIJ)	[56]
	6PEM	InvG	*S. enterica*	*N1/N0*	*3.5* Å	*16*	(SpaPQR:PrgHK)	[56]
	6Q14	InvG	*S. enterica*	*S/C/N3/N1/N0*	*3.8* Å	*15 (S/C/N3) 16 (N1/N0)*	(SpaPQR:PrgHK)	[56]
	6Q15	InvG	*S. enterica*	*S/C/N3/N1/N0*	*5.15* Å	*15 (S/C/N3) 16 (N1/N0)*	Open state (SpaPQR:PrgHIJK)	[56]
	6Q16	InvG	*S. enterica*	*N1/N0*	*4.1* Å	*16*	(SpaPQR:PrgHIJK)	[56]
	5TCQ	InvG	*S. enterica*	*S/C/N3*	*3.6* Å	*15*		[9]
	5TCR	InvG	*S. enterica*	*S/C/N3/N1/N0*	*6.3* Å	*15*	(PrgHK)	[9]
	7AHI	InvG	*S. enterica*	*S/C/N3/N1/N0*	*3.3* Å	*15 (S/C/N3) 16 (N1/N0)*	(SpaPQR:PrgHIJK: SptP)	[24]
	7AH9	InvG	*S. enterica*	*S/C/N3/N1/N0*	*3.3* Å	*15 (S/C/N3) 16 (N1/N0)*	(SpaPQR:PrgHIJK: SptP)	[24]
	6RWK	MxiD	*S. flexneri*	*N1/N0*	*3.86* Å	*16*	(MxiG)	[23]
T4P	6VE2	PilQ	*P. aeruginosa*	*C/N3*	*4.3* Å	*14*	(TsaP)	[21]
	6VE3	PilQ	*P. aeruginosa*	*C/N3*	*4.3* Å	*14*		[21]
	6VE4	PilQ	*P. aeruginosa*	*C/N3*	*6.9* Å	*15*		[21]
	6W6M	PilQ	*V. cholerae*	*C/N3/N0*	*2.7* Å	*14*		[30]
FPE	7OFH	pIV	F1 filamentous bacteriophage	C/N3	2.7 Å	15		[27]

Table1

Secretins for which a near-atomic resolution structure (<7Å) has been published is listed. For each structure, the name of the secretin and its organism of origin, its PDB entry, the stoichiometry, domains that are resolved and the overall resolution are indicated. When useful, additional information on specific features of the structure is provided.

Figure 1

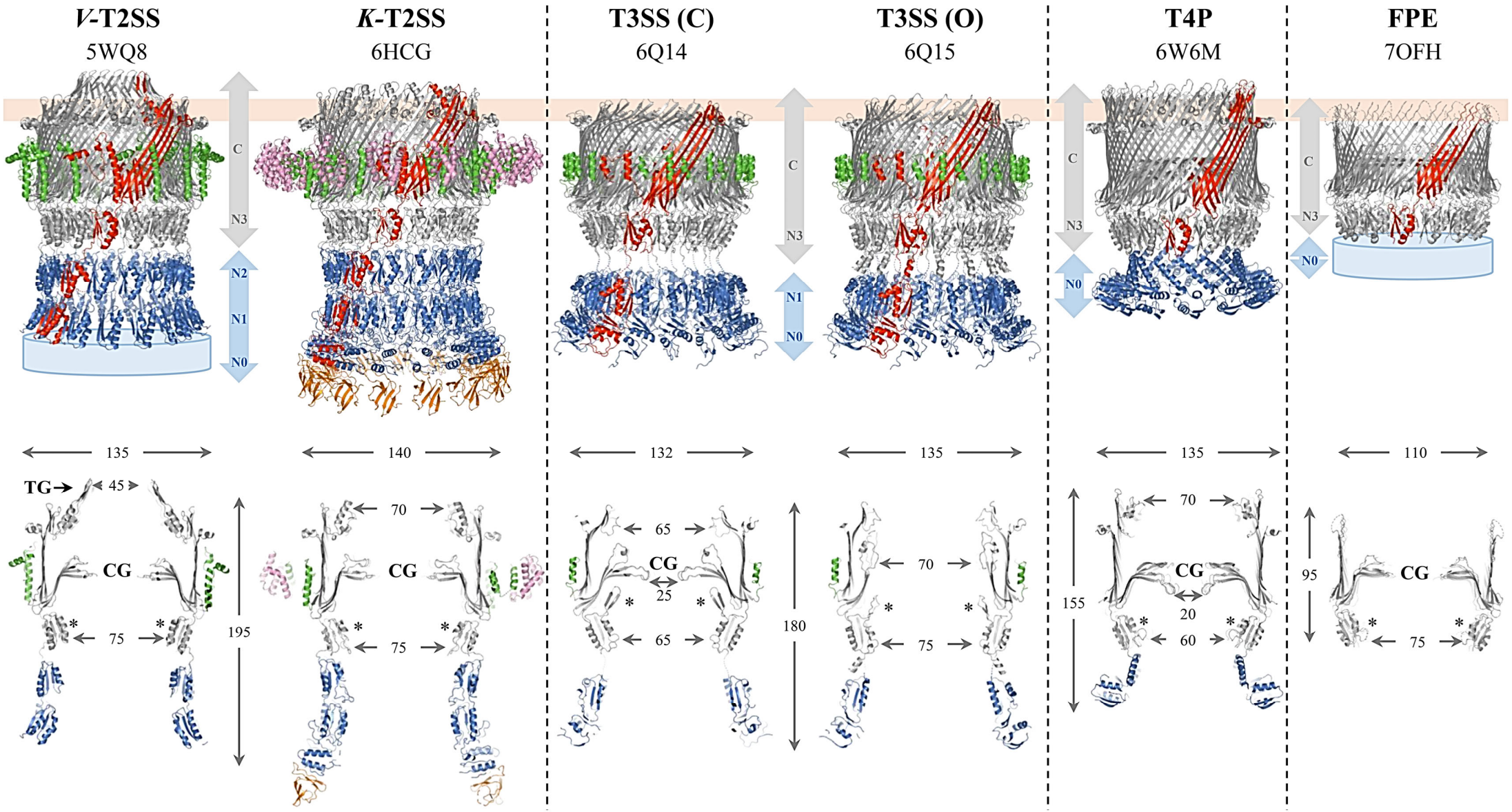
V-T2SS
5WQ8
K-T2SS
6HCG
T3SS (C)
6Q14
T3SS (O)
6Q15
T4P
6W6M
FPE
7OFH
C
N3
N2
N1
N0
135
140
132
135
135
110
TG
45
CG
75
195
70
65
25
180
20
60
155
95

Figure 2