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Review

Crossing the membrane in Archaea, the third domain of life☆

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A R T I C L E I N F O

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A B S T R A C T

Many of the recent advancements in the field of protein translocation, particularly from the structural perspective, have relied on Archaea. For instance, the solved structures of the translocon from the methanoarchaeon *Methanocaldococcus jannaschii* of the ribosomal large subunit from the haloarchaeon *Haloarcula marismortui* and of components of the SRP pathway from several archaeal species have provided novel insight into various aspects of the translocation event. Given the major contribution that Archaea have made to our understanding of how proteins enter and traverse membranes, it is surprising that relatively little is known of protein translocation in Archaea in comparison to the well-defined translocation pathways of Eukarya and Bacteria. What is known, however, points to archaeal translocation as comprising a mosaic of eukaryal and bacterial traits together with aspects of the process seemingly unique to this, the third domain of life. Here, current understanding of archaeal protein translocation is considered. This article is part of a Special Issue entitled Protein translocation across or insertion into membranes.

Contents

1. Introduction

Life on Earth is divided into three distinct domains, namely the Eukarya, the Bacteria and the Archaea [1]. Although it is now clear that Archaea are major denizens of so-called 'normal' environments, such as oceans, soil and even our own intestinal flora [2], Archaea remain best known as extremophiles, able to thrive in some of the most physically adverse conditions on the planet. As such, Archaea have been detected at extremes of pH, salinity, pressure and temperature [3].

Able to cope with environmental challenges for the most part not encountered by other life forms, it is not surprising that Archaea have come up with novel biological solutions to cope with their unique surroundings. The archaeal plasma membrane offers an example of one such domain-specific trait. The phospholipids that comprise the archaeal plasma membrane are composed of polyisoprenyl groups ether-linked to the *sn*-2,3 positions of a glycerol backbone and not the fatty acyl groups ester-linked to the *sn*-1,2 positions of glycerol that make up eukaryal and bacterial phospholipids [4,5]. It is believed that

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the ether bonds of the archaeal phospholipids would be more stable in the face of extreme environments. In addition, archaeal membranes may rely upon a monolayer structure composed of tetraether bipolar phospholipids, offering additional stability [6]. On the other hand, many aspects of archaeal biology find parallels in Bacteria and Eukarya. In terms of general traits related to protein translocation, Archaea resemble Bacteria morphologically, with both being surrounded by a plasma membrane enclosing a cytoplasm lacking organelles. On the other hand, protein translation in Archaea shows similarities to the eukaryal process, with ribosomes from the two domains showing similar antibiotic sensitivities [7].

While the study of Archaea has provided insight into strategies employed by Nature to cope with extreme environments, the related abilities of archaeal proteins and other cellular components to survive harsh conditions have also been exploited in structure-based studies aimed at enhancing our understanding of biological phenomena common to all organisms, yet not previously accessible for detailed analysis. At the same time, addressing the archaeal version of many biological processes has served to uncover unique solutions to problems encountered across evolution. In other instances, analysis of a given biological system from the archaeal perspective has served to link previously unrelated bacterial and eukaryal players. As described in this review, the study of protein translocation in Archaea has provided examples of each of these scenarios (Table 1).

2. Targeting

Before proteins can be translocated across the archaeal plasma membrane, they must first be correctly targeted. In Eukarya and Bacteria, the signal recognition particle (SRP) is responsible for delivering selected translating ribosomes to the membrane across which a given nascent polypeptide must cross, i.e., the membrane of the endoplasmic reticulum or the plasma membrane, respectively. Likewise, Archaea also contain SRP. However, despite the reported ability of archaeal SRP54 to interact with a signal sequence [8], experimental verification of a role for SRP in archaeal protein targeting and translocation remains lacking.

At first glance, the archaeal SRP is strikingly similar to its eukaryal counterpart, albeit simpler (Fig. 1). As in Eukarya, the archaeal SRP includes a 7S RNA molecule that assumes a secondary structure much like that seen in the eukaryal particle [9]. In addition, SRP19 and SRP54, two of the six protein components of the eukaryal SRP, are also part of the archaeal SRP. Nonetheless, aspects of SRP are unique to Archaea, with many of these domain-specific traits becoming apparent upon reconstitution of archaeal SRP from its purified components [8,10,11] as well as following structural examination of SRP, its sub-complexes or its individual components [12–20].

2.1. SRP RNA

Unlike the range of sizes seen with bacterial SRP RNA, archaeal SRP RNA contains on the order of 300 nucleotides, much like its human equivalent [9,21]. Likewise, eukaryal and archaeal SRP RNA contain seven helices each. Indeed, despite an overall lack of sequence conservation, archaeal SRP RNA can be folded into a secondary structure virtually identical to that of human SRP RNA, albeit with helix 1, formed upon pairing of the 5′ and 3′ ends of the molecule, being restricted to archaeal SRP RNA [9] and helix 7 only being found in the eukaryal molecule [22]. Helix 1 is, however, seen in *Bacillus subtilis* SRP RNA [23]. It is also of note that despite their phylogenetic and phenotypic diversity, archaeal SRP RNA molecules display striking similarities in even the finer details of secondary structure, including the position and sizes of internal loops within helix 5, the major backbone of the molecule.

2.2. SRP19

SRP reconstitution studies have shown that as in Eukarya, SRP19 plays a role in SRP assembly in Archaea, interacting with SRP RNA to facilitate SRP54 binding [8,10]. However, in contrast to the situation in Eukarya, the interaction between SRP RNA and SRP54 is not entirely SRP19-dependent in Archaea, with significant amounts of SRP RNA-SRP54 binding occurring in the absence of SRP19 [8,11,24]. Indeed, in *Haloferax volcanii*, the gene encoding SRP19 can be deleted without any apparent effect on cell growth, membrane protein insertion, protein secretion or ribosome levels [25]. The ability of SRP RNA and SRP54 to interact in the absence of SRP19 could reflect the need of Archaea for a stable SRP, given the environmental challenges that these microorganisms can encounter [10].

Addressing archaeal SRP19 binding to SRP RNA offers the opportunity to assess the contribution of SRP19 to SRP assembly. Accordingly, the results of various studies, including the biochemical description of the binding of *Archaeoglobus fulgidus* SRP19 to a fragment of SRP RNA comprising helices 6 and 8 [26] and structural analysis of *Methanocaldococcus jannaschii* SRP19 in complex with SRP RNA helix 5 and/or

Table 1
Sec pathway-mediated protein translocation across evolution.

	Archaea	Bacteria	Eukarya
Membrane lipids	polyisoprenyl ether-linked *sn*-2,3 to glycerol	fatty acyl groups ester-linked *sn*-1,2 to glycerol	fatty acyl groups ester-linked *sn*-1,2 to glycerol
Targeting			
Co- or post-translational?	post-translational secretion co-translational membrane protein insertion	post-translational secretion co-translational membrane protein insertion	co-translational secretion and membrane protein insertion (post-translational secretion possible in yeast)
SRP	7S RNA, SRP19, SRP54	4.5S RNA, Ffh	7S RNA, SRP9, SRP14, SRP19, SRP54, SRP68, SRP72
SRP receptor	FtsY	FtsY	SRα, SRβ
Targeting chaperones	unknown	SecB	Hsp70 (for post-translational secretion in yeast)
Translocon			
Core components	SecYEβ	SecYEG	Sec61αβγ
Auxiliary components	SecDF, YidC (?)	SecDFyajC, YidC	TRAM, Sec62/Sec63
Driving force of translocation	for secretion, unknown for membrane proteins, nascent polypeptide elongation (?)	SecA ATPase activity proton motive force nascent polypeptide elongation	nascent polypeptide elongation Hsp70 and BiP ATPase activity for post-translational secretion in yeast
Signal peptidase			
Oligomeric state	Monomer	Monomer	Multimer
Catalytic residues	Ser-His or Ser-His-Asp	Ser-Lys	Ser-His or Ser-His-Asp

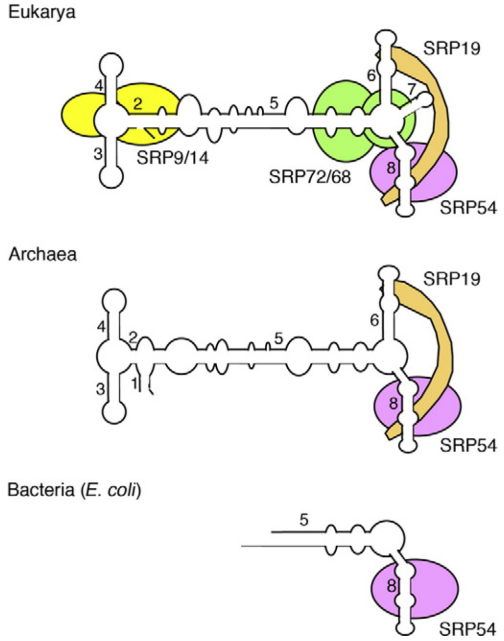

Fig. 1. SRP across evolution. Schematic depiction of eukaryal (human), archaeal and bacterial (*E. coli*) SRP are presented. The numbered helices of SRP RNA are indicated.

helices 6 and 8 [13,16], have revealed that archaeal SRP19 binds to the tips of SRP RNA helices 6 and 8 to induce a conformation change in the latter that, in turn, promotes SRP54 binding [10,13,14,16,19].

2.3. SRP54

SRP54 is responsible for binding the signal sequence of a nascent polypeptide chain emerging from the ribosome, as well as for interacting with the SRP receptor. As in the other two domains of life, SRP54 is an essential protein in Archaea [27]. SRP54 can be functionally divided into the C-terminal M region, involved in signal sequence recognition and SRP RNA binding, and the NG region, responsible for the guanidine nucleotide binding activity of the protein [28,29]. Analysis of the SRP54 M or NG regions, as well as of the intact protein, from a number of archaeal species has offered insight into the behavior of this central SRP component from the structural perspective. For instance, the structures of *Methanocaldococcus jannaschii* and *Pyrococcus furiosus* SRP54 have shown that the sequence linking the M and NG regions can assume a variety of conformations, apparently allowing the signal peptide-binding domain to engage diverse signal sequences as they emerge from the ribosome and regulating the activity of the NG region by coupling the two physically distinct yet functionally connected SRP54 domains [14,19].

2.4. FtsY, the SRP receptor

Whereas the archaeal SRP is reminiscent of its eukaryal counterpart, Archaea, like Bacteria, rely on FtsY as their SRP receptor. However, the manner by which archaeal FtsY associates with the membrane remains unclear, as does the significance of a substantial cytoplasmic FtsY pool. FtsY can be functionally divided into the N-terminal A region and the C-terminal NG region. The FtsY NG region, responsible for GTP binding [30], is well conserved in Archaea [31], while the archaeal FtsY A regions differ significantly in length and amino acid composition. Clusters of lysines and/or arginines are, nonetheless, found at the start of the archaeal FtsY A region [32], where they may act to link FtsY to anionic phospholipids of the plasma membrane, as proposed for the N-terminal region of the bacterial protein [33–35]. On the other hand, studies on the NG region of *H. volcanii* FtsY have shown that this portion is able to attach to the membrane [32,36], although the full protein was needed to mediate membrane association of SRP54 [32]. It is not clear whether this arrangement is true for all archaeal FtsY proteins or reflective of the relatively poor basic amino acid content of haloarchaeal proteins.

3. Archaeal protein translocation: A co- or post-translational event?

Across evolution, differences in the temporal relationship between protein translation and protein translocation are seen. In Bacteria, signal peptide-bearing secreted protein precursors are translocated post-translationally, i.e., once most, if not all, of the protein has been first translated in the cytoplasm [37,38]. In Eukarya, translocation of secretory preproteins across the membrane of the endoplasmic reticulum occurs co-translationally, in a SRP-dependent manner [39,40]. Accumulating evidence points to a co-translational mode of insertion for bacterial membrane proteins [41], while post-translational translocation has been reported in yeast [42]. Although limited in number, examples of both co-translational and post-translational translocation in Archaea are also available and are discussed below.

Of the studies addressing the relationship between archaeal protein translation and translocation, most have considered the biosynthesis of bacterioopsin, the multi-spanning *Halobacterium salinarum* membrane protein that serves as the apoprotein of the light-driven proton pump, bacteriorhodopsin. Co-translational insertion of bacterioopsin was first proposed based on the co-sedimentation of 7S (SRP) RNA and bacterioopsin mRNA together with membrane-bound polysomes, as well as on the basis of puromycin-induced release of 7S RNA from these polysomes [43]. Subsequent experiments reported the co-translational insertion of the N-terminal region of bacterioopsin and the post-translational insertion of the C-terminal portion of the protein [44,45]. On the other hand, membrane insertion of a cellulose-binding domain-tagged version of bacterioopsin heterologously expressed in *H. volcanii* required expression of the last transmembrane domain of bacterioopsin, indicative of a fully post-translational mode of insertion [46]. Still, it is important to note that bacterioopsin does not represent a standard membrane protein in terms of its membrane insertion. Bacterioopsin is synthesized with an unusually short, 13 residue cleavable signal peptide lacking a hydrophobic core yet containing negatively charged glutamate residues [43,47], unlike most signal peptides, where a positively charged region is followed by a hydrophobic core and a region containing the cleavage site [48,49]. As such, studies relying on bacterioopsin as a reporter of the temporal relation between translation and translocation in Archaea may not reflect the general situation. Indeed, given the importance of bacterioopsin in the generation of 'purple membranes,' a two-dimensional membrane protein lattice that forms in *Hbt. salinarum* in response to anaerobic and phototrophic conditions [50], a dedicated system for bacterioopsin membrane insertion may exist. Accordingly, more general support for co-translational membrane protein insertion in Archaea has come from addressing the relation between membrane-bound ribosomes and membrane protein biogenesis in *H. volcanii* [51]. In these studies, decreased ribosome membrane binding was shown to occur in cells expressing sterically blocked translocons, concomitant with a selective decrease in membrane protein integration.

The coordination between the translation and translocation of membrane proteins in Archaea may not, however, necessarily hold true for secreted proteins. Kinetic radiolabeling experiments performed with *H. volcanii* cells transformed to express SP-CBD, a chimeric preprotein comprising the signal peptide of the surface layer glycoprotein (the major exported protein in *H. volcanii*) fused to the cellulose-binding domain of the *Clostridium thermocellum* cellulosome, revealed that secretion of SP-CBD occurred only after translation of this reporter [52]. Moreover, an arrest of protein translation failed to prevent secretion of previously radiolabeled SP-CBD. Likewise, a proposed SecB homologue in *M. jannaschii*, reported to possess chaperone activity, has been suggested to correspond to a component of an archaeal post-translation translocational pathway [53]. Finally, as considered below, the archaeal Tat system apparently also translocates secretory preproteins in a post-translocational manner [27].

Hence, despite the relatively limited amount of data available, it is nonetheless tempting to speculate that in general, archaeal protein secretion occurs post-translationally, while membrane insertion in Archaea occurs co-translationally, in a SRP-dependent manner.

4. The archaeal Sec translocon

The solution of the three dimensional structure of the *M. jannaschii* Sec translocon in 2004 [54] led the workers in the field to realize that Archaea could serve as a powerful model system for addressing this central component of the translocation apparatus. However, the first indication that studying the Sec translocon from an archaeal perspective could provide unique insight into the process of protein translocation came when the homology between bacterial SecE and eukaryal Sec61γ, previously thought to be distinct proteins, was revealed through examination of the *Sulfolobus solfataricus* version of SecE [55]. Once the sequence similarity of archaeal SecE to eukaryal Sec61γ and the similar genomic organization of regions including the archaeal and bacterial SecE-encoding genes were realized, the universality of this translocon component became evident. On the other hand, analysis of archaeal genomes or individually isolated proteins had already revealed the similarities of archaeal and bacterial SecY to eukaryal Sec61α, with the archaeal protein more closely resembling its eukaryal rather than its bacterial homologue [56]. The complementation of a temperature-sensitive *Escherichia coli secY* mutant with the *Methanococcus vanielii* SecY-encoding gene showed, moreover, that not only could archaeal SecY functionally replace its bacterial counterpart but that the archaeal protein was functional even in the absence of the unique ether-based phospholipids that comprise the archaeal membrane [57].

In Bacteria, the core SecYE complex is accompanied by a third component, SecG [58,59], while eukaryal Sec61αγ exists in complex with Sec61β [60]. Unlike SecY and Sec61α or SecE and Sec61γ, SecG and Sec61β do not show significant sequence homology [61,62]. For this reason, no archaeal version of either SecG or Sec61β was originally reported [63,64]. Indeed, only after careful bioinformatics-based searches was the archaeal version of Sec61β identified [65].

The Sec61αβγ/YEG translocon has been shown to be associated with additional components. For instance, the eukaryal Sec61αβγ complex can be captured with TRAM [66] or the Sec62/63 complex [67], while in Bacteria, SecYEG can be isolated with SecDFyajC [68] or YidC [69]. Although no archaeal versions of the eukaryal auxiliary translocon components have been identified [64,70], analysis of available archaeal genomes reveals the presence of genes encoding homologues of SecDF and YidC. While the true physiological role of SecDF remains elusive, different functions have been assigned to the protein, including modulating the behavior of SecA, the ATPase that drives post-translational protein translocation in Bacteria [71,72]. As no archaeal version of SecA has been identified [63,64], it is unlikely that archaeal SecDF would serve any SecA-related function, as is attributed to its bacterial counterpart. Nonetheless, archaeal SecDF participate in Sec-mediated translocation, as reflected in the effects on protein export observed upon deletion of *H. volcanii secDF* [73].

While bacterial and archaeal SecDF present similar membrane topologies and organization of conserved sequence elements, closer examination reveals sequence differences along bacterial–archaeal lines [74]. Such differences are most obvious in SecD domain 2, situated in the large extracytoplasmic loop of the protein. It is tempting to speculate that such sequence differences reflect functional differences between bacterial and archaeal SecDF and hence between the translocation process in the two domains. Nonetheless, the analogous membrane topologies of bacterial and archaeal SecD and SecF, together with the adjacent positioning of their encoding genes in both cases, suggest that the *secD* and *secF* genes arose prior to the separation of the two domains. With time, however, the archaeal and bacterial versions of *secDF* diverged, reflected in the distinct phylogenetic separation of bacterial and archaeal SecDF. Furthermore, Archaea apparently do not encode YajC [62,74], a small protein in complex with bacterial SecDF [68].

Along with SecDF, the bacterial SecYEG complex can be also be co-isolated with YidC [69], shown to participate in the insertion of certain proteins into the bacterial plasma membrane [75]. Phylogenetic analysis has proposed the existence of members of the YidC/Oxa/Alb3 family of proteins in some but not all Archaea [76,77]. Experimental verification that the identified archaeal sequences functionally correspond to YidC homologues has, however, yet to appear. In fact, although the putative archaeal YidC proteins are predicted to assume a topology similar to that of their bacterial counterparts, the archaeal proteins are generally shorter and show only limited sequence homology to their bacterial homologues [76,77].

5. The archaeal Tat pathway

In addition to elements of the Sec translocation pathway, Archaea also encode for components of the Tat pathway [70]. Current understanding of the role of the Tat pathway in Archaea is largely based on surveys of completed genomes that predict differing extents of usage of this translocation system [78]. While the Sec pathway is thought to be the main route of protein translocation in the majority of archaeal species, the Tat pathway is believed to be the predominant mode of translocation employed by halophilic archaea [27,79]. Indeed, the preferred use of the Tat translocation pathway in halophilic archaea is reflected in the reported use of this route by not only soluble proteins but also C-terminally anchored membrane proteins and lipoproteins [80]. While it was originally proposed that the enhanced reliance of haloarchaea on the Tat pathway, where substrates are first folded and only then translocated, serves as a strategy to overcome potential dangers of protein misfolding in the hypersaline environments which haloarchaea inhabit [81], it has since been shown that the extremely halophilic bacterium *Salinibacter ruber* encodes SecA and is predicted to export proteins primarily via the Sec translocation pathway [82], where substrates are translocated prior to being folded. As such, alternative explanations for the apparent preference of haloarchaea for the Tat pathway are called for.

Whereas Archaea seemingly do not encode for the TatB subunit, genome analysis reveals the presence of TatA and TatC homologues in many but not all Archaea [78,83]. To date, studies of the archaeal Tat pathway at the molecular level have been conducted in halophilic archaea. Possibly related to their predicted preference for the Tat translocation pathway, haloarchaea express a dimer comprising fused TatC1 and TatC2 subunits, with the genes encoding each subunit being essential [81,84]. *H. volcanii* also contains two TatA-encoding genes, one of which is essential [81]. However, there seems to be little correlation between the number of Tat pathway components encoded by a given archaeal species and the predicted extent of usage of this pathway. For example, despite the predicted absence of Tat system substrates in *Methanopyrus kandleri*, the presence of at least one Tat component is suggested [78]. Finally, it has been reported that the haloarchaeal Tat pathway relies on the sodium motive force to power the delivery of pathway substrates across the membrane rather than the proton motive force, as employed by the bacterial and chloroplast Tat pathways [85].

6. Signal peptidase

Type I signal peptidases are integral membrane proteins responsible for the removal of signal peptides from preproteins at some stage during or following their translocation [86,87]. While tending to share little overall resemblance, signal peptidases in Eukarya and Bacteria include five regions of significant sequence homology, termed boxes A–E, with boxes B–E participating in the catalytic cycle of the enzyme (Fig. 2). Nonetheless, bacterial and eukaryal signal peptidases differ enzymatically and structurally. In the bacterial enzyme, the box B region contains the conserved nucleophilic Ser-90 (*E. coli* numbering) residue, while the proposed general base Lys-145 is found in box D. Ser-90 and Lys-145 are believed to form the catalytic dyad responsible for the proteolytic action of the enzyme [88]. It should be noted, however, that in a limited number of Gram-positive bacterial signal peptidases, e.g. *B. subtilis* SipW, the lysine residue of the catalytic dyad has also been replaced by a histidine, although a lysine could be introduced at this position without compromising enzymatic activity [89]. By contrast, eukaryal signal peptidases have replaced the essential lysine of the bacterial catalytic dyad with a histidine residue [90]. Thus, while their precise mode of action remains to be elucidated, eukaryal signal peptidases may rely on either a Ser-His dyad or a Ser-His-Asp triad for catalytic activity rather than the Ser-Lys dyad generally employed by the bacterial enzyme. The yeast signal peptidase Sec11 also contains two essential aspartic acid residues (the equivalents of *E. coli* Asp-273 and Asp-280), neither of which is required by the *E. coli* enzyme [91]. Finally, the bacterial and eukaryal enzymes also differ in terms of their oligomeric status. Unlike the bacterial enzyme, which functions independently, i.e., as a single encoded polypeptide, eukaryal signal peptidases function as part of a multimeric signal peptidase complex [92].

Examination of the archaeal signal peptidase indicates that it corresponds to an evolutionary intermediate between the eukaryal and bacterial enzymes [93,94]. While also containing sequence boxes A–E, archaeal signal peptidases lack the conserved lysine of the bacterial Ser-Lys catalytic dyad, instead containing a histidine residue at this position, as do eukaryal signal peptidases [93,95,96]. Thus, archaeal signal peptidases may rely on a catalytic mechanism similar to that used by the eukaryal enzyme. Indeed, site-directed mutagenesis studies of signal peptidases from *Methanococcus voltae* and *H. volcanii* have confirmed the essential nature of the equivalents of *E. coli* Ser-90 and His-145 in the archaeal enzymes [97,98], as is also true for the eukaryal enzyme [90]. Nonetheless, differences between eukaryal and archaeal signal peptidases exist. While the equivalents of the well-conserved Asp-273 and Asp-280 residues (*E. coli* numbering) are essential for the activity of the yeast enzyme [90], only the latter is essential for *M. voltae* and *H. volcanii* signal peptidase activity [97,98]. The role assumed by the Asp-280 equivalent in the catalytic mechanism of the archaeal enzyme is, however, unclear, since not all archaeal signal peptidases contain this residue [94,97]. The availability of an in vitro assay for Sec11b, one of the two versions of signal peptidase expressed by *H. volcanii*, should help address this and other mechanistic aspects of the archaeal enzyme [99]. Indeed, of the two *H. volcanii* signal peptidases, only Sec11b is apparently essential, given the inability to generate a chromosomal deletion strain lacking the encoding gene [99].

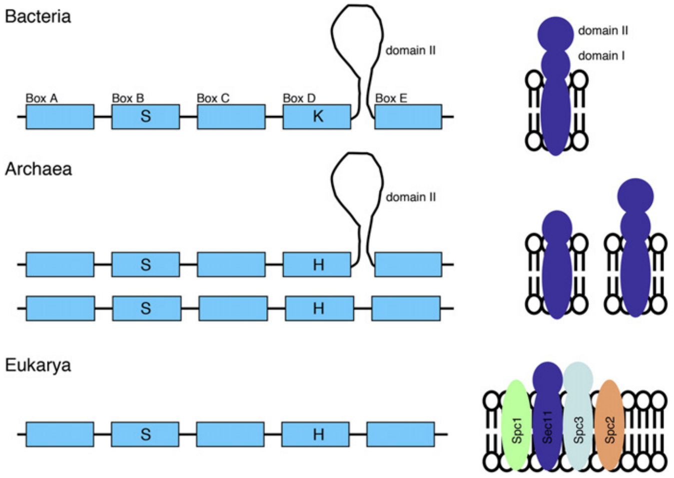

Fig. 2. Signal peptidase across evolution. Schematic depiction of bacterial (*E. coli*), archaeal and eukaryal (canine) signal peptidases are presented. In each case, the conserved sequence boxes A–E are depicted. In the bacterial and some archaeal signal peptidases, an additional sequence between boxes D and E, i.e., domain II, is detected. Domain I corresponds to the catalytic core of the enzyme. On the right, the oligomeric status of signal peptidase across evolution is shown; the bacterial and archaeal enzymes are monomers while the eukaryal enzyme is an oligomer comprising the catalytic Sec11 subunit together with Spc1, Spc2 and Spc3 subunits.

Finally, similarities between archaeal and bacterial signal peptidases also exist. The inability of genomic searches to thus far detect Eukarya-like signal peptidase complex subunits in Archaea suggests that the archaeal enzyme operates independently, as in Bacteria [93,94]. Furthermore, certain archaeal signal peptidases (such as in *Thermoplasma* species) include a stretch of residues that comprises domain II, a large β-sheet structure of unknown function positioned on top of the catalytic core (domain I) of the bacterial enzyme but not found in eukaryal signal peptidases [93,100]. Moreover, the same archaeal signal peptidases do not contain the Asp-280 equivalent shown to be involved in the catalytic activity of the *M. voltae* and *H. volcanii* enzymes, instead expressing a serine at this position, possibly equivalent to Ser-278, shown to be needed for optimal activity of the *E. coli* signal peptidase [94].

7. Concluding remarks

Although relatively recent and limited in number, studies into protein translocation from the archaeal perspective have had major impact on the field. What is known of archaeal protein translocation often confirms the mosaic nature of archaeal biology. This is emphasized by the fact that archaeal protein translocation implicates components not originally identified as being shared by the parallel eukaryal and bacterial systems, namely SecE/Sec61γ. Elsewhere, Archaea rely on components seemingly representing an intermediate between their bacterial and eukaryal counterparts, as exemplified by the archaeal SRP or signal peptidase. In yet other instances, such as in the Tat pathway, aspects of translocation apparently unique to Archaea are noted. The on-going development of improved molecular tools for working with archaeal strains growing across a range of environmental conditions ensures that these unusual microorganisms will continue to augment our understanding of protein translocation.

While Archaea have proven their value in elucidating mechanistic aspects of the translocation process, it has been their usefulness in

Table 2
Protein translocation pathway components crystallized from Archaea.

Component	Source	Comments	Reference
SecYEβ	*Methanocaldococcus jannaschii*		[54]
SRP	*Methanocaldococcus jannaschii*	Includes SRP RNA, SRP19, SRP54	[15]
SRP54	*Pyrococcus furiosus*		[19]
	Sulfolobus solfataricus	With and without SRP RNA helix 8	[18]
	Acidianus ambivalens	Only NG region	[12]
SRP19	*Pyrococcus furiosus*		[19]
	Archaeglobus fulgidus		[17]
	Methanocaldococcus jannaschii	With SRP RNA helices 6 and 8	[13,16]
SRP RNA	*Methanocaldococcus jannaschii*		[12]
FtsY	*Pyrococcus furiosus*		[20]
Ribosome	*Haloarcula marismortui*	50S subunit	[101]

structural studies that has generated the most interest from the translocation community. With 3D structures now available for the archaeal ribosome 50S subunit, SRP and its receptor and the translocon, Archaea have provided unparalleled insight into protein translocation (Table 2). Future efforts aimed at co-crystallizing different archaeal translocation components guarantee that Archaea will remain important models for deciphering how protein are delivered into and across biological membranes.

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