



Figure 1. Intramolecular O6,N7-chelate of guanine (right) to copper (green) and meridional N,N,O coordination of 2 guanines to copper.

Keywords: DNA, metal, supramolecular arrangement, copper(II)

MS7-P4 Signal sequence binding to the archaeal signal recognition particle

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The signal recognition particle (SRP) co-translationally targets proteins to the endoplasmic reticulum in eukaryotes or to the plasma membrane in prokaryotes. As the initiating step, SRP binds to the N-terminal signal sequence of nascent secretory or membrane proteins as they emerge from the ribosome. The SRP-ribosome nascent chain complex is then targeted to the membrane through a GTP-dependent interaction with the SRP receptor (SR). The signal sequence is released from SRP and inserted into the translocon channel. Finally, GTP hydrolysis triggers the dissociation of SRP from SR, and SRP can start another cycle of protein targeting.

SRP composition varies in the three domains of life. However, the evolutionary conserved SRP core only comprises the SRP54 protein bound to the coaxial stacked helices 5 and 8 of SRP RNA. SRP54 comprises an N-terminal NG domain that interacts with SR and a C-terminal methionine-rich M domain that binds to the signal sequence. Signal-sequence binding in the SRP54 M domain must therefore be effectively communicated to the SRP54 NG domain for receptor interaction. We have determined the 2.9 Å crystal structure of unbound- and signal-sequence bound SRP forms, both present in the asymmetric unit. The structures provide evidence for a coupled binding and folding mechanism in which signal-sequence binding induces the concerted folding of the GM linker helix, the finger loop, and the C-terminal alpha helix α M6. This mechanism allows for a high degree of structural adaptability of the binding site and suggests how signal-sequence binding in the M domain is coupled to repositioning of the NG domain for accelerated receptor interaction. We propose that signal-sequence recognition via a disorder-to-order transition of multiple structural elements facilitates specific recognition of widely diverse signal sequences.

Keywords: signal recognition particle, SRP, crystal structure, signal peptide, archaea