Cell wall anchoring mechanisms in archaeal S-layer proteins

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S-layer proteins (SLPs) assemble into highly ordered surface lattices that are critical for maintaining cell envelope integrity and mediating environmental interactions. Commonly the two distinct functions – self assembly and attachment – are also structurally separated.

In this study, we investigated three homologous SLPs from archaea, focusing on the hypothesized attachment domain with additional self-assembly capability. Using structural models from SymProFold [1] as a starting point, we could successfully identify a ligand-binding pocket that led to the discovery of specific binding to N-acetyl-glucosamine, implicating a glycan-mediated anchoring mechanism. Crystallographic and biochemical analyses revealed that this domain also contributes to lattice self-assembly, confirming a dual role in both structural organization and cell surface tethering.

Our findings demonstrate the importance of integrative workflows combining predictive modeling with crystallography to reveal multifunctionality in protein domains, especially in systems where conventional annotation falls short.

[1] Buhlheller, C., Sagmeister, T., Grininger, C. et al. *SymProFold: Structural prediction of symmetrical biological assemblies*. Nat Commun 15, 8152 (2024). https://doi.org/10.1038/s41467-024-52138-3