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UNDERSTANDING BACTERIAL IRON TRANSPORT

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We present preliminary results of molecular dynamics (MD) simulations on a nanosecond timescale in a fully solvated lipid bilayer to probe the mechanism of the FepA bacterial iron transporter protein.

Gram negative bacteria transport nutrients into the periplasmic space using a unique class of outer membrane proteins. The crystal structures of three members of this class of porin-like proteins, FhuA, FecA and FepA from *E. coli*, have recently been determined, [1] and the related structure of the Vitamin B_{12} transporter BtuB is about to emerge. These bacterial transporters formed from a 22-stranded beta-barrel pose an intriguing challenge to our current understanding of the Fe^{3+} (and Vitamin B_{12}) transfer mechanism as the protein barrel interior is occluded by a globular N-terminal domain, the "cork", comprising about 150 aminoacid residues in the case of FepA. Whether the cork "unplugs" during transport or undergoes an important conformational change remains unknown.

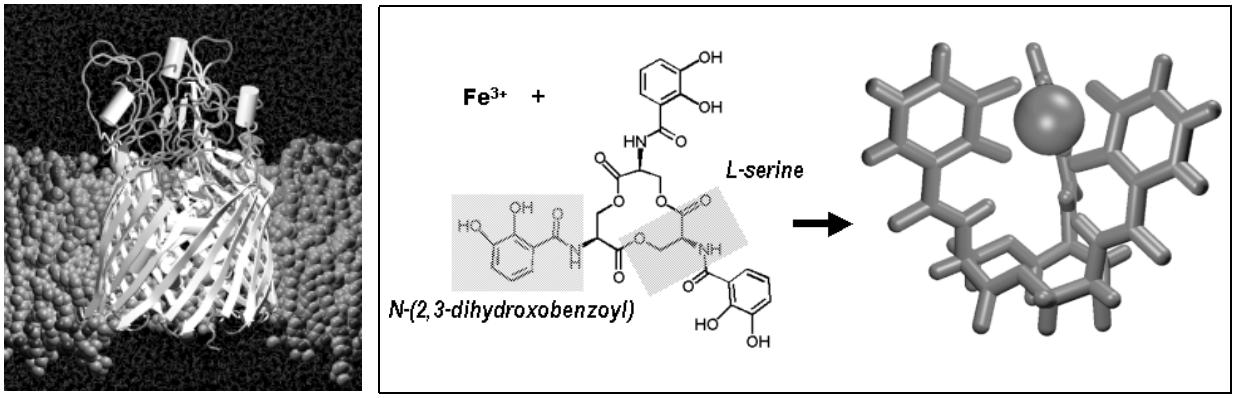

Figure 1. Left: A snapshot of the simulation system. FepA (white) embedded in a DMPC bilayer. Right : The enterobactin siderophore-iron complex, as transported by the FepA protein.

A detailed atomic picture of the iron transporter FepA emerges from our MD simulations (Fig. 1), providing insights into stable *vs* mobile parts of the structure and possible pathways of transport. Simulation data may furthermore be used to help interpret or confirm previous experimental measurements (*eg* EPR experiments) of other research groups. [2]

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[1] S. K. Buchanan *et al*, *Nature Struct. Biol.* **1999**, *6*, 56; A. D. Ferguson *et al*, *Science* **1998**, *282*, 2215; K. P. Locher *et al*, *Cell* **1998**, *95*, 771; A. D. Ferguson *et al*, *Science* **2002**, *295*, 1715.
[2] K. Bhargava *et al*, *Biophys. J.* **2002**, *82*, 2335.