BARRELS & CORKS IN A COMPUTER - MODELLING BACTERIAL IRON TRANSPORT SYSTEMS

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Gram negative bacteria transport nutrients into the periplasmic space using a unique class of outer membrane proteins. The crystal structures of two members of this class of porin-like proteins, FhuA and FepA from *E. coli*, have recently been determined. These iron transporters formed from a 22-stranded beta-barrel pose an intriguing challenge to our current understanding of the Fe transfer mechanism as the barrel is occluded by a globular N-terminal domain, the "cork", comprising about 150 aminoacid residues. Whether the cork "unplugs" during transport or undergoes a massive conformational change remains unknown. Understanding the molecular transport mechanism "in atomic detail" requires the use of a number of computational techniques. Homology modelling is used to obtain a full model of FepA, starting from the crystal structure, and pKa calculations shine light upon the most probable protonation state. Grand Canonical Monte Carlo simulations help address the hydration of the barrel interior. Molecular Dynamics simulations with explicit membrane models and solvent provide insight into the conformational dynamics of the system. The overall goal is a model of the protein and its environment which is accurate enough to reproduce the essential features of the system. (This work is supported by an EC Marie Curie Fellowship.)