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## Contents



# 1 Abstract


## 1.1 Modelling the FepA protein, a bacterial iron transporter in the outer membrane

FepA, the receptor for ferric enterobactin-iron in E. coli, is representative of a wider family of bacterial outer membrane proteins mediating the active transport of ferric siderophores through the outer membrane of Gram-negative bacteria (*Roosenberg 2000*).

Such transporters are possible targets for novel anti-bacterial drugs, as inhibition of transport could be used to impede bacterial growth. Although X-ray diffraction studies have provided a high resolution structure of FepA (*Buchanan et al.*), alternative approaches such as molecular dynamics (MD) simulations are needed to probe the conformational dynamics of this molecule, requiring an adequate all-atom model.

Starting from *Buchanan et al.*'s crystal structure, a complete atomistic model of the full FepA apoprotein is developed in several steps. Homology modelling is required to fix missing sidechains and residues, pKa calculations shine light upon the probable protonation state of ionizable residues, and Grand Canonical Monte Carlo simulations provide insight into the hydration of the barrel interior. The latter method is able to reproduce crystal waters and effectively predict water positions not resolved in the crystal structure, as well as to address the question of water density inside the pore.


### 1.1.1 References


Buchanan, S. K.; Smith, B. S.; Venkatramani, L.; Xia, D.; Essar, L.; Palnitkar, M.; Chakraborty, R.; van der Helm, D. and Deisenhofer, J.; 1999. Crystal structure of the outer membrane active transporter FepA from Escherichia coli. *Nature Struct. Biol.* **6**:56-63.

Roosenberg, J. M. 2nd; Lin, Y. M.; Lu, Y. and Miller, M. J.; 2000. Studies and syntheses of siderophores, microbial iron chelators, and analogs as potential drug delivery agents. *Curr. Med. Chem.* **7**:159-97.