β-lactam inhibitors permeability. The OmpF model

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Multidrug resistance in bacteria is a challenging problem that threatens contemporary medicine. Gram-negative bacteria are puzzling systems for drug discovery due to the presence of the outer membrane (OM). Porins are the main access to internal targets for polar antibiotics and a better understanding of the permeability mechanism is needed.

β-lactam antibiotics are a broad class of antibiotics that includes penicillin cephalosporins, and carbapenems. In this case permeation does not guarantee success due to the fact that bacteria often develops resistance against β-lactam antibiotics by synthetizing β-lactamases, enzymes that recognize and attack the β-lactam ring, rendering inactive this type of antibiotics.

The discovery of new compounds using different functional groups and with good permeability properties is very challenging. Though, the development of β-lactam inhibitors may play a key role, giving β-lactam antibiotics a second chance to fight bacteria. Inhibitors as well as polar antibiotics have to exploit the porin pathway in order to reach their target inside bacteria. Here we present an *in silico* study of five β-lactam inhibitors namely avibactam, sulbactam, tazobactam, bal0120275, and bal029880. Using metadynamics enhanced molecular dynamics simulations we investigated their permeability through OmpF. Permeability properties are highly correlated to electrostatics and for that reason OmpF, the most studied OM protein on *E. Coli*, serves as model for general porins.