Metadynamics simulations of fluoroquinolones translocation through the OmpC porin

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The rapidly spreading antimicrobial resistance in Gram-negative bacteria has been revealed as a major threat of the twenty first century. Poor outer membrane permeability is considered as one possible causes of the poor antibiotic activity. Not much is known about the permeation mechanisms for available antibiotics. Here, we investigate the transport mechanisms through the outer membrane porin OmpC of *E. coli* for two effective fluoroquinolone molecules, ciprofloxacin and enrofloxacin. To achieve this goal, we used metadynamics which is a powerful and well-established enhanced sampling method for exploring and quantifying free energy surfaces as a function of appropriately chosen variables. The reconstruction of the free energy landscapes allows for estimating the energy barriers and local minima encountered by the molecules during the translocation process. Furthermore, the string method helps to identify minimum transition paths in these free energy landscapes. A molecular level understanding of the translocation mechanisms can possibly guide the design of new antibiotics capable of achieving a high intracellular accumulation.