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Sugar transport through maltoporin of *Escherichia Coli*: A combined molecular dynamics and stochastic modeling approach

We investigate the energetics and the underlying physical mechanism of sugar molecule (glucose and maltodextrin) transport in the highly asymmetric maltoporin (LamB) outer membrane channel, from E. coli, by employing a combination of all atom molecular dynamics (MD) simulations and stochastic modeling approach. Although maltoporin is well characterized experimentally and its high resolution crystal structure has been known for a decade, no previous MD simulation studies of this porin have been reported. We use equilibrium MD simulations to investigate the conformational stability of maltoporin, and nonequilibrium steered molecular dynamics (SMD) simulation to facilitate and characterize the full permeation of a glucose molecule through the maltoporin channel. By employing a new analysis method developed in our group, we determine from fast SMD pulling simulations both the free energy profile (PMF) and the position dependent diffusion coefficient of the glucose molecule along the axis of the channel. Finally, these quantities are used as input in a stochastic model based on the Fokker-Planck equation that permits to describe the transport of the sugar molecule through the channel on a mesoscopic time scale that is inaccessible to current MD simulations. The obtained PMF is highly asymmetric and we argue that the cell may exploit the nonequilibrium fluctuations of the outer membrane to accelerate sugar uptake.