Séminaire

CONFÉRENCIER INVITÉ

Vendredi 20 Octobre 2017 à 11h

Salle des séminaires

Institut de biologie structurale - 71 avenue des Martyrs CS 10090 38044 Grenoble Cedex 9 - T.+33 (0)4 57 42 85 00

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From Chaperones to the Membrane with a BAM

Bacteria have an amazing ability to directionally sort outer membrane proteins (OMPs) in the absence of an external energy source such as ATP. We developed a computational model to understand how they accomplish this remarkable feat. This OMP Biogenesis Model – termed OmpBioM – integrates parameters from experiments both in vivo and in vitro. It incorporates all major periplasmic chaperones at their cellular concentrations, interaction rate constants and considers biological oligomeric states to predict the periplasmic lifetimes, copy numbers and sorting trajectories for OMPs. Using deterministic and stochastic methods we simulated OMP biogenesis under varying conditions replicating biochemical and genetic findings. OmpBioM stochastic simulations reveal that, on average, there are hundreds of binding and unbinding events between periplasmic chaperones and unfolded OMPs. These interactions are thermodynamically favored yet kinetically fast suggesting that the periplasmic conditions are near equilibrium with OMPs being “tossed” from chaperone to chaperone. Following equilibration in the periplasm, BAM catalyzed folding is the ultimate, rate-limiting step for OMP incorporation into bacterial outer membranes. Overall, we find a finely tuned balance between thermodynamic and kinetic potentials maximizes OMP folding flux, directs them to the correct membrane, and minimizes unnecessary degradation: a kinetic “push” prevents OMPs from incorporation into the wrong membrane; OMP sorting is random in the aqueous periplasm; and – once folded – OMPs are thermodynamically favored and kinetically trapped in their native conformations.

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