UniSysCat Colloquium

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Start Time: Wednesday, October 20, 2021 05:00 pm

End Time: Wednesday, October 20, 2021 06:00 pm

Computer simulations to predict ligand binding kinetics and diffusion rates

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The first step of enzyme catalysis is enzyme-substrate binding, a process that is characterized by binding kinetics and that depends on the diffusion rate of the substrate.

In the first part of the talk, I will explain why ligand binding kinetics is an emerging topic in drug design and I will show how molecular dynamics simulations and the tau-Random Acceleration Molecular Dynamics method can be used to characterize dissociation rate constants and obtain mechanistic insights about factors modulating binding kinetics in kinases and T4 lysozyme mutants.

In the second part of the talk, I will present evidence that the catalytic efficiency of TEM1 beta-lactamase is reduced in crowded cell-like environments. Then I will show how reduced diffusion rates of small molecules in the presence of protein crowders, obtained from Brownian dynamics simulations and fluorescence recovery after photobleaching, may help to explain this reduced catalytic efficiency.