# Nonequilibrium Molecular Dynamics of Trp Zwitterion in Water: Picosecond Fluorescence Measurements versus Computer Simulations.

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This is an experimental test of MD simulations on the picosecond timescale. Tryptophan zwitterion in TIP3P water at 278°K was simulated using CHARMM22 forcefield with the excited-state Trp atomic charges from [Toptygin et al., *J. Phys. Chem. B* **2010,** *114,* 11323]. Six stable excited-state rotamers of Trp sidechain were found with the population density peaks near ($\chi_1$,$\chi_2$) = (67°,80°), (-170°,57°), (-65°,115°), (65°,-85°), (-165°,-112°), (-65°,-80°). Curved boundaries between the rotamers on the ($\chi_1$,$\chi_2$) map were drawn along the troughs of the population density. Population density distribution within the boundaries of one rotamer reaches equilibrium in less than 20ps; equilibration between different rotamers takes much longer. At t>20ps rotamer populations can be described by a system of six first-order homogeneous linear differential equations. The solution is a sum of six terms $V_{mn}\exp(-t/\tau_n)$. Population decay of each rotamer is not monoexponential and $\tau_n$ is not a lifetime. The same set of $\tau_n$ applies to all rotamers, but a different set of $V_{mn}$ corresponds to each rotamer. The rotamers have slightly different fluorescence emission spectra, therefore fluorescence intensity is a sum of six terms $\alpha_n(\nu)\exp(-t/\tau_n)$, where $\alpha_n$ vary with the photon energy $h\nu$. We have determined $\tau_n$ and $\alpha_n(\nu)$ in the global analysis of spectrally- and time-resolved fluorescence data (time resolution 65ps FWHM). Only four exponential terms could be resolved from the experimental data in $H_2O$ at 5°C ($\tau_1$=4780ps, $\tau_2$=2500ps, $\tau_3$=867ps, $\tau_4$=411ps); according to MD simulations the fifth term ($\tau_5$=241ps) has a very small amplitude, and the sixth ($\tau_6$=22ps) is faster than the time resolution. For a precise agreement between the experimental and simulated values of $\tau_n$ it is necessary to lower all potential barriers between rotamers by 0.178kcal/mol. This shows that fluorescence spectroscopy can be used to fine-tune torsional parameters.

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