

[L14] Integrating molecular dynamics simulations and far-IR spectroscopy to study biomolecular dynamics

Roland H. Stote

Department of Integrative Structural Biology, Institut de Génétique et de Biologie Moléculaire et Cellulaire (IGBMC), INSERM U964 UMR 7104 CNRS, Université de Strasbourg, Illkirch, France

There is significant evidence that collective vibrational modes in the frequency range of 2 to 600 cm^{-1} can play significant roles in physiological processes such as allosteric signal transmission. Far-IR and terahertz (THz) spectroscopies, which can probe this low frequency region of the vibrational spectrum, are emerging as attractive techniques for studying such dynamical behavior, especially when combined with other methods such as molecular dynamics simulations.

In a recent study, we used such an integrative approach to study peptide binding by the second PDZ domain (PDZ1) of MAGI1. This PDZ domain has been identified as an important target for the Human Papilloma Virus. Both the experimental and calculated far-IR spectra showed a red shift of the low-frequency peaks of the PDZ upon peptide binding. The calculations showed that this is coincident with an increased number of hydrogen bonds formed as the peptide augments the protein β -sheet. We further identified the contribution of surface-bound water molecules to bands in the far-IR.

PDZ domains are of interest because of their importance in signaling events within the cell. They are frequently found in multidomain scaffold proteins where binding information is transferred between domains. Through the molecular dynamics simulations and subsequent analysis, we identified a potential mechanism of dynamic coupling of the N- and C-terminal ends, thus allowing us to quantify a mechanism of allostery in this PDZ domain. This study showed for the first time the potential of integrating molecular dynamics and far-IR studies to obtain a comprehensive description of the functional dynamics of proteins.

Reference

[1] Yoann Cote, Yves Nominé, Juan Ramirez, Petra Hellwig, Roland H. Stote, *Biophysical Journal*, Volume 112, Issue 12, 15 June 2017, 2575-2588, <http://dx.doi.org/10.1016/j.bpj.2017.05.018>