ChE SEMINAR

Ab initio Models for Lipid Mixtures and Misfolded Proteins

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ABSTRACT

Non-aqueous solvents are used to extract lipids and alcohols generated in the cytosol of algae for bioenergy. The cell colony membranes are exposed to hydrophobic solvents in their outer sides leading to cracks and holes in their phospholipid bilayers. Energetic cytosol compounds can then be extracted by leaking through the voids. Hydrocarbons are common extractors due to their high partition coefficients. With molecular dynamics (MD), the degradation of a phospholipid membrane by hexane, heptane and decane is simulated. In the model, the membrane is constituted by a periodic slice with the bilayers in the middle, water representing the cytosol in the bottom and external solvent in the top of the slice. Only hydrophobic and entropic non-covalent effects are sufficient to crack the membrane and drag out phospholipids into the solvent bulk after a short time of a few nanoseconds. By self-assembly, the escaped lipids can form nanoparticles (as reverse micelles) in the hydrophobic solvent. We observe by MD that the membrane is significantly degraded after exposition to the hydrocarbons, which may lead to cellular depth after extraction. For sustainability of the process, cellular death should be avoided by minimizing the defects induced to the membrane. Biocompatible surfactants coating the membrane outer side to limit the number of created voids by the "digging" solvent seem a plausible technology to avoid cellular depth.

The second part of my presentation concerns protein folding, a major bioscience problem. Misfolding is involved in a number of the most incurable and widespread pathologies as neurodegenerative diseases (Alzheimer and Parkinson, e.g.). In humans, the prions are the only known type of protein-only infection propagation by simple contact between normal PrP and toxic PrPsc configurations leading to amyloidoses and transmissible encephalopathies. Misfolding can happen in the entire prion (that is natively only semi-folded) while only an enzymatically-cleaved peptide sequence becomes misfolded in other brain diseases. Using classical and quantum molecular models, prion-prion docking and interactions are studied to prove the existence of stable misfolded isoforms, in contrast to the hydrophobic collapse theory to a unique folded state. In vitro, prions in fungi and yeast self-reproduce, with inherited phenotypes, from mother to daughter cells by self-assembly of amyloid aggregate patterns, which may seem paradoxical with the molecular biology dogma that the only genetic information carriers are nucleic acids.

ABOUT THE SPEAKER

Dr. Gillet is currently visiting professor at the Jawaharlal Nehru University in Delhi for the School of Computational and Integrative Sciences and Centre for Computational Biology and Bioinformatics. His recent research is focused on the development of ab initio molecular models, based on both classical and quantum methods, for numerical experimentations on the dynamics of biomolecules and organic compounds, as lipid - organic mixtures and protein folding and docking. Before his stay in J.N.U., Dr. Gillet was as well an active researcher in materials science and nanotechnology with high-impact publications. He received his Ph.D. in 2001 from Laval University in Canada. After he was associated for research with the "Ecole Polytechnique" in Montreal and University of Montreal's Hospital Centre. In 2007, he came to the "Ecole Centrale" in Paris, one of the three top engineering schools in France with "Ecole Polytechnique" and "Ecole des Mines". He has now twelve years of teaching and research academic experience after his Ph.D. graduation.