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# *S E M I N A I R E*

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## " Protein Folding and Dimerization on Ribosomes "

In this talk I will discuss the following problems:
1.Ribosome is a molecular machine for protein synthesis which involves four phases of translation - initiation, elongation, termination and ribosome recycling. This process is an area of intense research due to the essential role of proteins to life. Recently we have shown that electrostatic interactions govern extreme nascent protein ejection times from ribosomes and can delay ribosome recycling [1].
2.The hydrophobic interaction, which plays a key role in protein folding, was well studied in the aqueous environment. However, the water-mediated hydrophobic interaction inside the ribosome exit tunnel has been poorly understood. Using molecular dynamics simulation and umbrella sampling we showed that the hydrophobic effect is weaker in the vestibule. These findings mean that nascent proteins pass through a ribosome vestibule environment that can destabilize folded structures, which has the potential to influence co-translational protein folding pathways, energetics, and kinetics [2].
3. Using coarse-grain simulations of protein synthesis we showed that synonymous mutations can influence the protein dimerization in solution. The structural and kinetic origin of this effect is associated with misfolded states containing non-covalent lasso-entanglements, many of which structurally perturb the dimer interface, whose probability of occurrence depends on translation speed [3].

[1] D. A. Nissley, Q. V. Vu, F. Trovato, N. Ahmed, Y. Jiang, M. S. Li, and E. P. O'Brien, J. Am. Chem. Soc. 142, 13, 6103-6110 (2020).
[2] Q. V Vu, Y. Jiang, M. S. Li, E.P. O'Brien, Chemical Science 12, 11851 (2021).
[3] L. P. Dang, D. A. Nissley, I. Sitarik, Q. V. Van, Y. Jiang, M. S. Li, E. P. O'Brien, Synonymous mutations can alter protein dimerization through localized interface misfolding involving self-entanglements, doi: https://doi.org/10.1101/2021.10.26.465867.

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**14h30**

**Salle des conférences**