UNIVERSITY OF LOUISVILLE

COLLEGE OF ARTS & SCIENCES

Department of Chemistry

Brown and Williamson Series

Friday, January 21, 2022
@4:00 pm
Chemistry Building LL16

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Cobalamin: the cofactor enabling improbable chemistries

ABSTRACT:

We are interested in discovering how biological catalysts accomplish “unusual” or “improbable” chemistries. Our targets include vitamin B12 (cobalamin)-dependent enzymes such as methylmalonyl-CoA mutase (MCM) and methionine synthase (MS). B12 is one of nature’s most complex cofactors enabling and allowing for challenging chemistries to occur from bacteria to humans. In MCM, B12 utilizes radicals to enable an otherwise very challenging chemical reaction; the isomerization of methylmalonyl-CoA to succinyl-CoA. MS on the other hand is a multi-modular enzyme essential for folate and one carbon metabolism. MS catalyzes a challenging methyl transfer from methyltetrahydrofolate to homocysteine to form methionine and tetrahydrofolate. Our interest in MS stems from the chemically improbable methylation that it catalyzes, the unique capabilities of its cobalamin cofactor and its exceptional dynamic properties that support three chemically different methylation reactions. The goal of our work is to uncover fundamental principles regarding how enzyme dynamics facilitate challenging chemistries.

BIO:

Markos Koutmos is an Assistant Professor in the Department of Chemistry and Department of Biophysics. He is also affiliated with the University of Michigan Program in Chemical Biology and the Cancer Biology Program. He began his independent career at the Uniformed University of the Health Sciences and then moved to the University of Michigan in 2018. The Koutmos lab is interested in understanding how the 3D structure and dynamics of proteins and RNAs drive their biological function. His lab combines chemistry, biophysics and biology approaches to build a foundation of basic knowledge for understanding the remarkable chemistries catalyzed by nature’s best enzymes, uncovering the roles of biomacromolecules in disease, and discovering new classes of therapeutic targets. The Koutmos lab is specifically interested in metalloenzyme structure and function, in RNA modifications and processing, and in RNA structure and dynamics.