

## **Co-translational membrane protein folding in native lipid environments**

The folding of newly synthesised proteins to their correct structure is essential to attaining functionally normal proteins that are vital to health. The majority of folding research studies artificially-denatured, full-length chains - a situation that is unrepresentative of cellular folding. Although folding is a highly topical area of research, membrane proteins are a particularly understudied class. Nearly all alpha helical membrane proteins fold co-translationally during biosynthesis, as the ribosome is translating mRNA, with insertion being assisted by translocase apparatus. Thus, the proteins fold in the membrane during elongation of the polypeptide chain, and not as full-length chains. We have shown that a lipid membrane (devoid of translocase components) is sufficient for successful co-translational folding. Folding is spontaneous, thermodynamically driven, and the yield depends on lipid composition. We have highlighted how Infra-Red spectroscopy can be used to monitor co-translational folding in real time. We have also advanced our studies to native lipid compositions and the study of ribosome nascent chain complexes, where different length nascent chains are stalled whilst still attached to the ribosome.