

Abstract Submitted  
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**First step in folding of nonconstitutive membrane proteins: spontaneous insertion of a polypeptide into a lipid bilayer and formation of helical structure**<sup>1</sup> YANA RESHETNYAK, ALEXANDER KARABADZHAK, DHAMMIKA WEERAKKODY, Physics, URI, DONALD ENGELMAN, Yale Univ., VLADISLAV MARKIN, Univ of Texas Southwestern Med School, OLEG ANDREEV, Physics, URI — There are two questions we would like to address: 1) what is the molecular mechanism of a polypeptide insertion into a lipid bilayer and formation of transmembrane helix? 2) Are there any transient changes of a lipid bilayer in process of a polypeptide insertion and folding? As a convenient system we are studying pHLIP (pH (Low) Insertion Peptide) insertion into a membrane and folding, which is modulated by pH. The insertion of pHLIP occurs with rapid (0.1 sec) interfacial helix formation followed by a much slower (100 sec) insertion pathway to form a transmembrane helix. The reverse process of unfolding and peptide exit from the bilayer core proceeds much faster than folding/insertion and through different intermediate states. Our kinetic studies with pHLIP variants indicate that insertion can occur 100 times faster and with less number of intermediate states. To study changes, which might occur with a lipid bilayer in a process of peptide insertion and folding, we employed stopped-flow SAXS.

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