Abstract Submitted
for the NEF13 Meeting of
The American Physical Society

Membrane-associated folding: Polar cargo translocation across a lipid bilayer[1] DAYANJALI WIJESINGHE, OLEG ANDREEV, YANA RESHETNYAK, University of Rhode Island, BIOLOGICAL AND MEDICAL PHYSICS, URI TEAM — Here we present study of the mechanism of cargo translocation across a membrane by the single molecule transporter, pHLIP (pH (Low) Insertion Peptide). The main principle of this drug delivery approach is based on the phenomenon of the pH-dependent insertion and folding of moderately hydrophobic membrane peptides. Several pHLIP variants were used to probe the delivery of cargoes of different polarities attached to the peptide inserting end. While the equilibrium thermodynamics favor the binding and insertion of the pHLIP-cargo constructs, the kinetics was significantly slowed down. The presence of a polar cargo at the peptide's inserting end leads to the appearance of two additional intermediate states on the insertion pathway of the pHLIP-2E, which itself (when no cargo is attached) shows an all-or-none transition from the partially unstructured membrane-surface state to the transmembrane state. Our findings are very valuable for the design of new delivery agents for the direct translocation of polar cargo across a membrane. To facilitate the different delivery needs for different applications the hydrophobicity of the cargo could be modified without affecting the cargo's ability to bind to its cellular target (shown by us previously) and/or various peptides of the pHLIP family could be employed, which show different rates and pKa of a cargo's translocation across cellular membranes.

[1]This work was supported by a NIH grant CA133890 to OAA, YRK

Dayanjali Wijesinghe
University of Rhode Island

Date submitted: 13 Sep 2013 Electronic form version 1.4