# From single-molecule protein unfolding to protein degradation by the proteasome

P03-03

**A. Aguado**[I], P. Matín[I], D. Fernández[I], D. Rodríguez-Larrea[I]

[I]Biofisika Institute, Leioa, Spain

Biological nanopores are frequently found within many biological structures involved in protein folding/unfolding. In the case of the proteasome, protein degradation requires unfolding and translocation of protein substrates through a narrow pore into the internal catalytic chamber. How protein stability relates to protein degradation remains an unsolved question. Single molecule approaches using protein nanopores with dimensions comparable to the size of the proteasome have the potential to provide insight into the underlying physics of the process. Here we measure the kinetics and energy consumption of the bacterial proteasome ClpXP during degradation of a battery of mutants of SsrA-tagged thioredoxins. Single-molecule measurements of protein unfolding during translocation through the α-hemolysin pore were expected to show excellent correlation with protein degradation because both unfold proteins by pulling the polypeptide chain through nanometer scale pores. Our results show a lack of correlation between nanopore induced protein unfolding and ClpXP protein degradation. This suggests that the unfolding observed during protein degradation may be more complicated than a mere one-end pulling unfolding mechanism.