Single-molecule evidence of Entropic Pulling by Hsp70 chaperones

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Hsp70 chaperones are central components of the cellular network that ensures the structural quality of proteins. Despite crucial roles in processes such as protein disaggregation and protein translocation into organelles, their physical mechanism of action has remained hotly debated. To the best of our knowledge, no experimental data has directly proven any of the models proposed to date (Power Stroke, Brownian Ratchet, or Entropic Pulling) due to a lack of suitable methods. Here, we use nanopores, a powerful single-molecule tool, to investigate the mechanism of Hsp70s. We demonstrate that Hsp70s extract trapped polypeptide substrates from the nanopore by generating strong forces (equivalent to 46 pN over distances of 1 nm), that rely on the size of Hsp70. The findings provide unambiguous evidence of the Entropic Pulling mechanism, thus solving a long-standing debate, and proposing a potentially universal principle governing diverse cellular processes. Additionally, these results highlight the utility of biological nanopores for protein studies.

Reference:

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