ATOMISTIC SIMULATION OF SINGLE MOLECULE EXPERIMENTS: MOLECULAR MACHINES AND A DYNASOME PERSPECTIVE

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Proteins are biological nanomachines which operate at many length and time scales. We combined single molecule, x-ray crystallographic, and cryo-EM data with atomistic simulations to elucidate how these functions are performed at the molecular level. Examples include the mechanics of energy conversion in F-ATP synthase and tRNA translocation within the ribosome. We will show that tRNA translocation between A, P, and E sites is rate limiting, and identified dominant interactions. We also show that the so-called L1 stalk actively drives tRNA translocation, and that 'polygamic' interactions dominate the intersubunit interface, thus explaining the detailed interaction free energy balance required to maintain both controlled affinity and fast translation We will further demonstrate how atomistic simulations enable one to mimic, one-to-one, single molecule FRET distance measurements, and thereby to markedly enhance their resolution and accuracy. We will, finally, take a more global view on the 'universe' of protein dynamics motion patterns and demonstrate that a systematic coverage of this 'dynasome' allows one to predict protein function.

[1] Puchner EM, Alexandrovich A, Kho AL, Hensen U, Schafer LV, Brandmeier B, Grater F, Grubmuller H, Gaub HE, Gautel, *PNAS* 105 (2008), 13385.
[2] Böckmann R, Grubmüller H., *Nature Struct. Biol.* 9 (2002),198.
[3] Czub J and Grubmüller H., *PNAS* 108 (2011), 7408.
[4] Wozniak AK, Schroder GF, Grubmuller H, Seidel CA, Oesterhelt F., *PNAS* 105 (2008), 18337.
[5] Hoefling M, Lima N, Haenni D, Seidel CAM, Schuler B, Grubmüller H., *PLoS ONE* 6 (2011), e19791.
[6] Hensen U, Meyer T, Haas J, Rex R, Vriend G, Grubmüller H., *PLoS ONE* 7 (2012), e33931.
[7] Bock LV, Blau C, Schröder GF, Davydov II, Fischer N, Stark H, Rodnina MV, Vaiana AC, Grubmüller H., *Nature Struct. Molec. Biol.* 20 (12) (2013), 1390-1396.

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