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Title:	Anisotropy in mechanical unfolding of protein upon partner-assisted pulling and handle-assisted pulling
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Abstract:	Proteins as force-sensors respond to mechanical cues and regulate signaling in physiology. Proteins commonly connect the source and response points of mechanical cues in two conformations, independent proteins in end-to-end geometry and protein complexes in handshake geometry. The force-responsive property of independent proteins in end-to-end geometry is studied extensively using single-molecule force spectroscopy (SMFS). The physiological significance of the complex conformations in force-sensing is often disregarded as mere surge protectors. However, with the potential of force-steering, protein complexes possess a distinct mechano-responsive property over individual force-sensors. To decipher, we choose a force-sensing protein, cadherin-23, from tip-link complex and perform SMFS using end-to-end geometry and handshake complex geometry. We measure higher force-resilience of cadherin-23 with preferential shorter extensions in handshake mode of pulling over the direct mode. The handshake geometry drives the force-response of cadherin-23 through different potential-energy landscapes than direct pulling. Analysis of the dynamic network structure of cadherin-23 under tension indicates narrow force-distributions among residues in cadherin-23 in direct pulling, resulting in low force-dissipation paths and low resilience to force. Overall, the distinct and superior mechanical responses of cadherin-23 in handshake geometry than single protein geometry highlight a probable evolutionary drive of protein-protein complexes as force-conveyors over independent ones.
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