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Dynamic Similarities in Pathological Forms of α-Synuclein RYAN BRADLEY, University of Pennsylvania, JANNA MARANAS, Pennsylvania State University — The natively unstructured, membrane-bound protein α-synuclein is thought to play a role in vesicle trafficking. Its native function is subverted in the pathogenesis of Parkinson's disease, during which it forms fibrillar cytoplasmic aggregates in specific regions in the brain. It is believed that oligomers of α-synuclein are the toxic species, whereas sequestration into fibrils is neuroprotective. Evidence that α-synuclein changes shape as it interacts with membranes suggests that altered dynamics may drive the initial aggregation steps. To test this hypothesis, we conducted separate molecular dynamics simulations of native, mutated, and chemically-damaged forms of α-synuclein, representing the distinct genetic and sporadic causes of the disease. We measured the fractal dimension of individual amino-acid trajectories in order to identify differences in mobility between each simulated protein. Trajectories with higher fractal dimensions are space-filling, and thus correspond to more random, constrained motion; conversely, lower fractal dimensions indicate more directed motions. Although the disease-causing variants of α-synuclein are distinct, they show highly similar dynamical differences from the native form. This suggests that altered dynamics may facilitate oligomerization.

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