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Crowded, cell-like environment induces shape changes in aspherical protein¹

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How the crowded environment inside cells affects the structures of proteins with aspherical shapes is a vital question because many proteins and protein–protein complexes *in vivo* adopt anisotropic shapes. Here we address this question by combining computational and experimental studies of a football-shaped protein (i.e. *Borrelia burgdorferi* VlsE) under crowded, cell-like conditions. The results show that macromolecular crowding affects protein-folding dynamics as well as overall protein shape. In crowded milieus, distinct conformational changes in VlsE are accompanied by secondary structure alterations that lead to exposure of a hidden antigenic region. Our work demonstrates the malleability of “native” proteins and implies that crowding-induced shape changes may be important for protein function and malfunction *in vivo*.

¹In collaboration with Dirar Homouz, University of Houston; Michael Perham, Rice University; Antonios Samiotakis, University of Houston; and Pernilla Wittung-Stafshede, Umea University.