

Role of protein flexibility in gramicidin A channel permeability

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Proteins have a flexible structure, and their atoms exhibit considerable fluctuations under normal operating conditions. However, apart from some enzyme reactions involving ligand binding, our understanding of the role of flexibility in protein function remains mostly incomplete. Here we investigate this question in the realm of membrane proteins that form ion channels. Specifically, we consider ion permeation in the gramicidin A channel (GA), and study how the energetics of ion conduction changes as the channel structure is progressively changed from fixed NMR structure to a completely flexible one as obtained from molecular dynamics (MD) simulations. For each channel structure, the potential of mean force for a permeating potassium ion is determined from MD simulations. Using the same MD data for completely flexible gramicidin A, we also calculate the average densities and fluctuations of the GA atoms and investigate the correlations between these fluctuations and the motion of a permeating ion. Our results show conclusively that peptide flexibility plays an important role in ion permeation in the gramicidin A channel, and hence it cannot be modeled using continuum electrostatics with an average, fixed structure.