Cyclic Conformational Changes in GPCR Revealed by Normal Mode Analysis

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In G protein signaling, the initial step of binding of activated receptor with Gs protein α -subunit (G α s) causes the release of GDP from a biding pocket located between Ras-like GTPase domain (G α sRas) and α -helical domain (G α sAH). These allosteric reactions occur accompanying by the conformational change of G α s protein from the closed GDP binding state to the fully opened GDP unbinding one. Elastic network model based normal mode analysis describes the whole conformational change event of G α s. It suggests that receptor binding of G α s which is also determined sequentially from N to C terminal would break the dense connection between G α sRas and G α sAH, leading to their collective motion that increases the GDP solvent-accessible surface area. Furthermore, we propose a feasible intermediate state between closed and open form of G α s with GDP/GTP exchange, which enables to complete the whole signal transduction cycle of G protein.

Keywords: GPCR, G Protein, Normal Mode Analysis, Elastic Network Model