Dynamics of G-Protein Coupled Receptor (GPCR) Activation and Attenuation: Insights from Fluorescence Studies.

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"When rhodopsin is activated, do the helices go up and down, or do they move sideways"? Gobind Khorana asked me this when I first joined his lab. Seventeen years later, I am still working on a version of his question: What specific structural changes occur in GPCRs when they are activated, and how do these changes provide a mechanism for transducing signal across the membrane?

My talk will mainly focus on insights that fluorescence studies have given us about the interaction of GPCRs with various ligands, G-proteins and arrestins. However, I will also discuss a novel fluorescence method we developed for our studies, which we call the Tryptophan Induced Quenching (TrIQ) method. We recently determined that using the TrIQ method, we can identify sites of direct fluorophores-Trp contact in proteins, and importantly, precisely quantify the amount of these interactions, on a nanosecond timescale. Thus, I will review how fluorescence methods, such as our TrIQ method, have provided insights into where helical movements occur in GPCRs, and how these movements act to enable coupling with GPCR affiliated proteins.