

Scientific Lecture – Garland R. Marshall

Cation- π Interactions: Are They Worth Their Salt? Probing the Interface Between Photoactivated Rhodopsin and Its G-Protein.

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Interactions between cationic and aromatic side chains of amino acid residues, the so-called cation- π interactions, are thought to contribute to the overall stability of the folded structures of peptides and proteins [1]. The transferred NOE NMR structure [2] of the Gt_R(340-350) peptide bound to photoactivated rhodopsin (R*) geometrically suggested a cation- π interaction stabilizing the structure between the ϵ -amine of Lys341 and the aromatic ring of the C-terminal residue, Phe350. This interaction has been explored by varying substituents on the phenyl ring of Phe350 to alter the electron density, and observing the impact on binding of the peptide to R*. The results [3] suggest that while a cation- π interaction geometrically exists in the Gt_R(340-350) peptide when bound to R*, its energetic contribution to the stability of the receptor-bound structure is relatively insignificant, as it was not observed experimentally. The presence of an adjacent and competing salt-bridge interaction between the ϵ -amine of Lys341 and the C-terminal carboxylate of Phe350 effectively shields the charge of the ammonium group. Experimental data supporting a significant cation- π interaction can be regained through a series of Phe350 analogs where the C-terminal carboxyl was converted to the neutral carboxamide, thus eliminating the shielding salt bridge. TrNOE NMR experiments confirmed the existence of a cation- π interactions of the Gt_R(340-350) analogs in the carboxamide analogs [3]. Various literature estimates of the strength of cation- π interactions, including some that estimate strengths in excess of salt bridges [4, 5], are compromised by omission of the relevant anion in the quantum calculations. Similar calculations of the Gt_R(340-350) peptide analogs bound to R* do not overestimate the strength of the cation- π interaction.

References:

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