# The role of hydrophobic matching on transmembrane helix packing in biological membranes

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**B. Grau**[I], M.J. García-Murria[I], I. Mingarro[I], L. Martínez-Gil[I]

[I]Departament de Bioquímica i Biologia Molecular, ERI BioTecMed, Universitat de València, Burjassot, Spain

The concept of Hydrophobic matching refers to the pairing between hydrophobic core of the membrane (MB) and the transmembrane (TM) domain of the protein, in order to avoid unfavorable exposure of hydrophobic surfaces to a hydrophilic environment. Hydrophobic matching was been widely studied experimentally and computationally.
Glycophorin A (GpA), which represent one of the best suited and most studied models for helical transmembrane (TM) segment packing and MB protein folding, has been used as *in vitro* experiment for understand Hydrophobic matching, showing that the surrounding hydrophobic environment length can modify the GpA TM segment dimer/monomer equilibrium. However, there is not, up to date, a direct confirmation of this effect and its implication on MB protein folding *in vivo*.
In this work we explore the concept of hydrophobic matching *in vivo* using chimeric GpA proteins with different length TM domain. Results show, equally in *Escherichia coli* cells (Tox RED assay) and human derived cells (BiFC assay), in contrast to previous *in vitro* studies, that all tested chimeric proteins can homo-dimerize through the TM domain in an *in vivo* context, concluding that biological membranes can accommodate transmembrane homo-dimers with a wide range of hydrophobic lenghts. Furthermore, hetero-dimers with a large length disparity between their monomers were also tolerated. Nonetheless, length differences between transmembrane helices hindered the dimer/monomer equilibrium confirming the impact of the hydrophobic matching on helix packing *in vivo*.