

An operational model for GPCR homodimers and its application in the analysis of biased signaling

Bin Zhou, Institut de Neurociències & Unitat de Bioestadística (UAB)
E-mail address: bin.v.zhou@gmail.com.

G protein-coupled receptors (GPCRs) are among the most important protein superfamilies as drug targets in drug discovery programs. Their interactions with ligands are influenced by their homomerization. In this study, we propose an operational model for receptor homodimers, which includes constitutive receptor activity. Distinct functional response curves can be obtained from this model, which can satisfactorily depict typical complex experimental data as biphasic and bell-shaped curves. Operational parameters in the model may provide mechanistic explanations for observed functional complexity associated with the cooperativity and intrinsic efficacy of ligands. Because the herein presented model is derived within the conceptual framework of operational models, it takes advantage of the body of knowledge coming from the widespread use of this type of modeling. The operational homodimer model can also explain the biased signaling dependent on ligand concentration. In conclusion, this operational homodimer model has a wide range of applications in pharmacological research.

This is a joint work with Jesús Giraldo.