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GPCR activation: An intertwined history of crystallography and EM

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G-protein coupled receptors (GPCRs) remain the most successful class of drug targets. However, only a small subset of human GPCR structures have been solved to date. Of those, GPCRs in complex with the effector G-protein are particularly recalcitrant to crystallisation.
Single particle EM played a key role in determining the crystal structure of a ligand-receptor-G-protein ternary complex [1,2]. Advances in phase plate cryo-EM have shown that high-resolution structure determination of small protein complexes is facile by single particle analysis [3].
Here, we present a staged development process for structure determination of intricate membrane protein complexes, highlighting complementary strengths of crystallography and cryo-EM.
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[2] Westfield et al., 2012, PNAS, 108, 16086-91
[3] Khoshouei et al., 2016, bioRxiv, doi: https://doi.org/10.1101/087841
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