



**Figure 1. Structure of the GluK2/K5 heteromer in a resting state**

**(A)** Cryo-EM structure of the GluK2/K5 heteromer in a CNQX-bound state with GluK2 and GluK5 subunits rendered in green and blue, respectively. The micelle is shown as a silhouette. **(B and C)** Molecular model for the receptor colored as in (A) and shown from two different views parallel to the membrane. The off-axis tilt of the ATD layer is indicated in (C). **(D-F)** The three layers of the GluK2/K5 heteromer as viewed from the extracellular space. The local symmetries of the ATD (D, two-fold), LBD (E, two-fold), and TMD (F, four-fold) are illustrated. **(G)** Typical responses (1 mM L-Glu, 1 ms application) evoked by GluK2 and GluK2/K5 receptors in external NaCl, LiCl or CsCl solutions. **(H)** Summary of relative amplitudes for GluK2 and GluK2/K5 receptors in various external ions. Amplitudes are percentages relative to NaCl. **(I)** The fast component of deactivation kinetics ( $\tau_{fast}$ ) for GluK2 and GluK2/K5 receptors in various external ions. **(J)** Scatter plot of data fit by linear regression comparing response amplitude and deactivation kinetics for GluK2 and GluK2/K5 receptors in different external ion conditions. See also Figures S1-S6.