Bilayer clamp experimental details.

The methodology was derived from that previously described (*1*). A model BC-525A bilayer clamp (Warner Instrument Corp.) was used for all planar bilayer experiments, ClampEx 8 and ClampFit 10 (Axon Instruments) were the software used for acquisition and analysis, respectively. Cups used were made of polystyrene and had 250µm diameter apertures. The lipid used in all cases was diphytanoyl phosphatidylcholine (diPhyPC) (Avanti Polar lipids). A stock solution of 25mg/mL lipid in $CHCl_3$ was dried under N_2 and then re-suspended in 200µL decane. For compounds that had to be pre-loaded into the lipid, 0.1 – 1mol% compound in $CHCl_3$ was added to the lipid mix and then dried down. The electrolytes used were 1M KCl, NaCl, CsCl, or NMe_4Cl in 10mM HEPES, 10mM TRIS, pH 7, (unadjusted).

The aperture was primed with 0.5-1µL of decane/lipid, excess solvent was removed by blowing N_2 over the aperture. The cup was then placed into the electrolyte-filled holding cell, consisting of 5mL and 3mL chambers, and salt bridges (KNO_3/Agar) and electrodes (Ag/AgCl) were attached. Bilayers were formed by brushing on 1- 1.5µL of the decane/lipid mix over the aperture, and were monitored for stability, capacitance and resistance for at least 20 minutes before test compound was added. Test compounds were added by injection from an organic solution (typically no more than 1-10µL of solution) or by breaking the lipid-only bilayer and brushing on the compound-preloaded in a lipid mix. All data were hardware filtered (8- pole Bessel filter, 1 kHz) and data was collected in a survey mode using the Gap-free protocol. Bilayers were tested repeatedly for capacitance and resistance. Once formed, 'activity' from pristine bilayers was never observed.

Conductance data summary format.

Each experiment conducted is summarized in a separate file within this portfolio. The structure of each summary is similar consisting of:

- A title of the form: file identifier {date} [compound] details of the experiment
- A plot of the applied potential as a function of the overall experiment time. Color overlays on this plot show the durations of the recorded traces, numbered sequentially 0000 – 00mn. The plot also shows when bilayer breakage occurred (if it did).
- A bar graphic showing the composition of the experiment as it proceeded. The lines establish that the indicated component was continuously present.
- Activity grid summaries for the individual traces recorded. These grids use the notation presented in ref (*2*). The horizontal position gives event duration in log (duration) from 1 to 10^5 millieconds. The vertical position gives conductance in log (conductance) from 1 to 3000 pS in 0.5 log unit steps (1,3,10,30 etc pS). The colour codes are : green = regular "square-top behaviour; yellow = "flicker" behaviour; blue = "multiple open states" behaviour; red = "spike" behaviour; purple = "erratic" behaviour; grey indicates the region cannot be observed due to the instrument and data processing settings of the experiment .
- For each trace recorded there are one or more pages showing the overall trace and selected sections expanded to highlight the various conductance behaviours noted on the activity grid for the experiment.

(1) Eggers, P.K.; Fyles, T.M.; Mitchell, K.D.D.; Sutherland, T., *J. Org. Chem.* **2003,** *68*, 1050-1058.

(2) Chui, J.K.W.; Fyles, T.M., *Chem. Soc. Rev.* **2011** DOI: 10.1039/c1cs15099e.