$$I_{rel}(c) = \frac{I_{act}(c)}{I_{act}(0.1\,mM\ ATP^{4-})}$$

$$= \frac{I_{rel,\infty,1}}{\left(1+\frac{10^{-\log K_{D1}}}{c}\right)^2} + \frac{I_{rel,\infty,2}}{\left(1+\frac{10^{-\log K_{D2}}}{c}\right)^2}$$

Fig S3. Modeling of P2X7 receptor affinity for ATP. Approximation of the concentration-dependence of ATP4--evoked currents by a model of two equal high-affinity and two equal low-affinity non-cooperative activating binding sites 11 25. The current Iact(c) activated after 6 s application of different concentrations c of ATP4- or BzTP4- was normalized to the respective current at 1 mM ATP4- (Iact(0.1 mM ATP4-)) to yield Irel(c). Irel, ,1 and I rel, ,2 are the maximal relative current components contributing to Irel(c) after saturating at infinite concentrations of the agonist the binding sites with the apparent dissociation constants KD1 and KD2, respectively. The coefficient of 2 gave higher correlation coefficients than models using one, three or more equal binding sites, respectively. pKD1 = 6.1?±1.3 and pKD2=3.7?±0.1 were calculated.