Supporting Information

for

Determination of Structures and Binding Energies of Europium Complexes Bound to Biologically Relevant Anions

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Note S1: Derivation of relation for binding energy

The detailed derivations for the section 2.3 of the manuscript are provided here. The reaction scheme in equation S1 is used to compute binding energies. The term $\mathrm{Eu \cdot L{-}H_2O}$ shows the europium ion bound to ligands (L) and a water molecule H_2O. The anionic species acting as guest G^- replaces the water molecule from $\mathrm{Eu \cdot L{-}H_2O}$ to form the host-guest complex $\mathrm{Eu \cdot L{-}G^-}$.

$$\mathrm{Eu \cdot L{-}H_2O + G^- \rightleftharpoons Eu \cdot L{-}G^- + H_2O} \tag{S1}$$

Following this reaction scheme, the binding free energy is defined as

$$\Delta G_b^{\ominus} = G^{\ominus}(\mathrm{Eu \cdot L{-}G^-}) + G^{\ominus}(\mathrm{H_2O}) - G^{\ominus}(\mathrm{Eu \cdot L{-}H_2O}) - G^{\ominus}(\mathrm{G^-}) \tag{S2}$$

where $G(X)$ represents the free energy of component X.

The binding energy is related to the binding constant K_b by

$$\Delta G_b^{\ominus} = -RT \ln K_b \tag{S3}$$

At equilibrium, K_b connects the concentration of host-guest complex [Eu-G], water [H_2O], host-water complex [Eu-H_2O] and guest [G] via

$$K_b = \frac{[\mathrm{Eu \cdot L{-}G^-}][\mathrm{H_2O}]}{[\mathrm{Eu \cdot L{-}H_2O}][G^-]} \tag{S4}$$

To simplify this equation, we first eliminate the formal explicit dependence on the water concentration by defining a new equilibrium constant as follows

$$K_b^o = \frac{K_b}{[\mathrm{H_2O}]} = \frac{[\mathrm{Eu \cdot L{-}G^-}]}{[\mathrm{Eu \cdot L{-}H_2O}][\mathrm{G^-}]} \tag{S5}$$

Furthermore, in practice, it is not always clear whether the guest is present in its deprotonated (G^-) or protonated forms (HG). We, thus, define an apparent binding constant (K_b') with respect to the total concentration of guest independent of its protonation state

$$K_b' = \frac{[\mathrm{Eu \cdot L{-}G^-}]}{[\mathrm{Eu \cdot L{-}H_2O}]([\mathrm{G^-}] + [\mathrm{HG}])} \tag{S6}$$

$$\frac{1}{K_b'} = \frac{[\mathrm{Eu \cdot L{-}H_2O}]([\mathrm{G^-}])}{[\mathrm{Eu \cdot L{-}G^-}]} + \frac{[\mathrm{Eu \cdot L{-}H_2O}]([\mathrm{HG}])}{[\mathrm{Eu \cdot L{-}G^-}]} \tag{S7}$$

To further simplify this expression, we need the acid dissociation constant (K_a) of the guest:

$$\mathrm{HG \rightleftharpoons H^+ + G^-} \tag{S8}$$

$$K_a = \frac{[\mathrm{H^+}][\mathrm{G^-}]}{[\mathrm{HG}]} \tag{S9}$$

Substituting Eq. (S5) into the left part of Eq. (S7) and Eq. (S9) in the right part, we obtain

$$\frac{1}{K_b'} = \frac{1}{K_b^o} + \frac{[\mathrm{Eu \cdot L{-}H_2O}]([\mathrm{H^+}][\mathrm{G^-}])}{[\mathrm{Eu \cdot L{-}G^-}]K_a} \tag{S10}$$

$$\frac{1}{K_b'} = \frac{1}{K_b^o}(1 + \frac{[\mathrm{H^+}]}{K_a}) \tag{S11}$$

$$K_b^o = K_b'(1 + \frac{[\mathrm{H^+}]}{K_a}) \tag{S12}$$

$$K_b = [\mathrm{H_2O}]K_b'(1 + \frac{[\mathrm{H^+}]}{K_a}) \tag{S13}$$

$$\Delta G_b^{\ominus} = -RT \ln[\mathrm{H_2O}] - RT \ln\left(1 + \frac{[\mathrm{H^+}]}{K_a}\right) - RT \ln K_b' \tag{S14}$$

Eq. (S14) gives the free energy, which has been corrected for the concentration of water and pH. Practically, we evaluate the experimental binding free energy via Eq. (S14) using experimentally determined apparent binding constants K_b'. We evaluate the computational binding free energy via Eq. (S2) using free energies from a standard rigid-rotor/harmonic-oscillator model.

S2: Additional figures for anion binding section

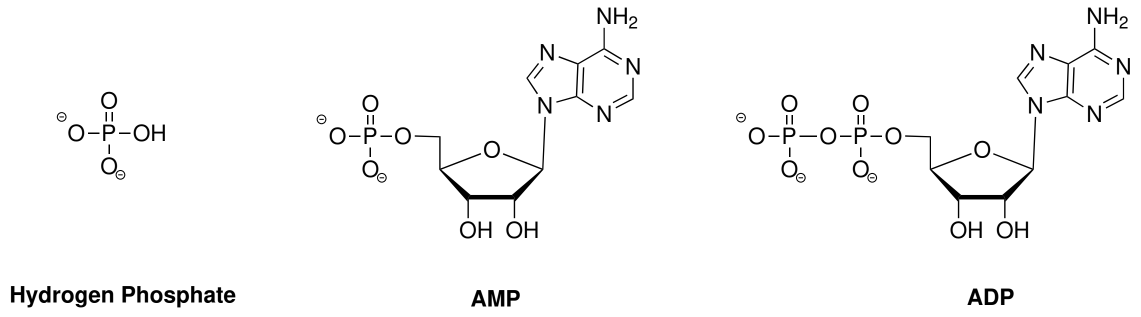

Figure S1: Structures of the anions studied.

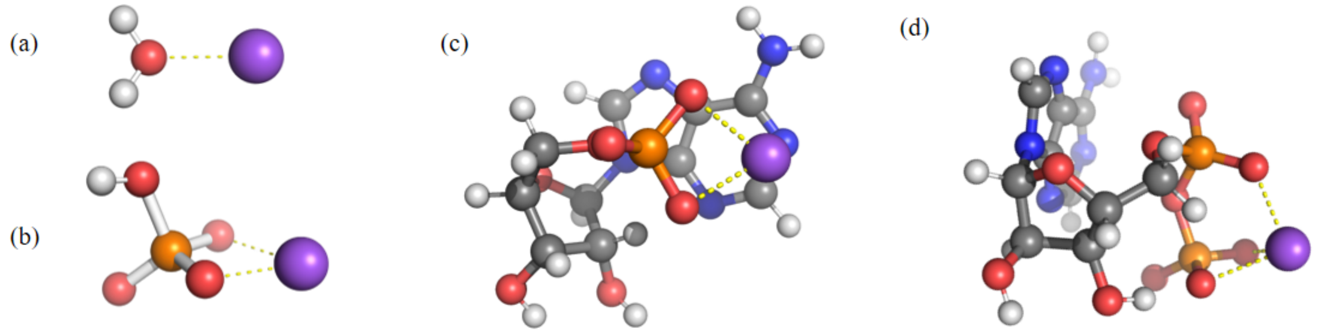

Figure S2: Sodium cation (represented by the purple sphere) complexated with (a) water, (b) hydrogen phosphate, (c) AMP, and (d) ADP.

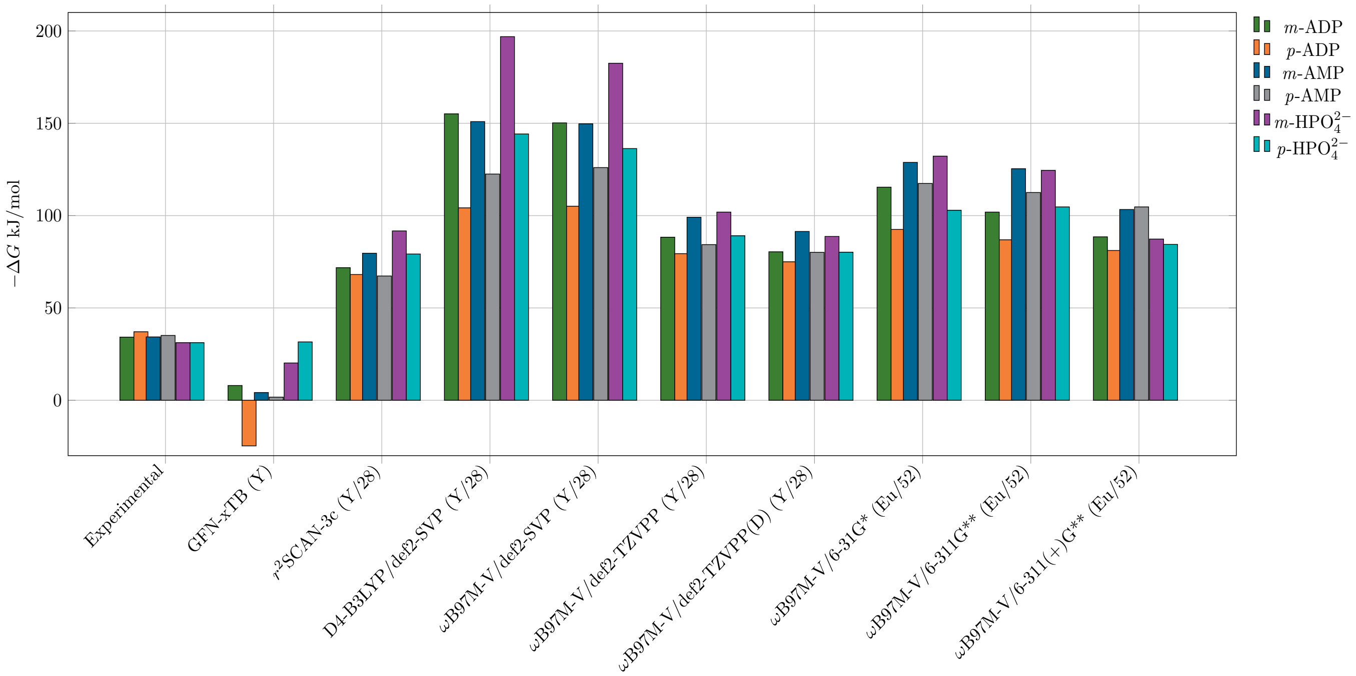

Figure S3: Binding free energies of anions (without Na^+ complexation) with europium complexes determined with different methods.

Data availability

Additional data for this article (input, output and coordinate files for all computations performed) are available at Loughborough University's institutional repository at
`https://doi.org/10.17028/rd.lboro.31281982`.