# Supporting Information

## Supporting Text

Acetonitrile was distilled under nitrogen from calcium hydride. Chloroform was distilled under nitrogen from calcium chloride. All other solvents and chemicals were commercially available and used without further purification. Silica 60 (Merck) was used for silica gel chromatography. NMR spectra were taken on a Varian Inova 400 (400 MHz, $^1$H and 2D spectra) or on a Bruker DMX300 (75 MHz, 13C spectra) and calibrated to an internal standard of tetramethylsilane. Abbreviations used: s, singlet; d, doublet; t, triplet; bs, broad singlet. Fluorescence experiments were performed on a PerkinElmer LS50B luminescence spectrometer equipped with a thermostatted cuvette holder. UV-vis spectra were recorded on a Cary 100 Conc (Varian) UV-Vis spectrometer.
Porphyrin macrocycle **Zn1** (1), dimethyl viologen **V1** (2) and scaffold **3** used in the synthesis of **V2** (3) were synthesised according to literature procedures.

**Synthesis. 4-(*tert*-butyl-diphenyl-silanyloxymethyl)pyridine (A1).** 4-pyridylcarbinol (1.0 g, 9.2 mmol) and imidazole (1.0 g, 14.7 mmol), were dissolved in 50 mL of $CH_2Cl_2$, and to this solution was slowly added tert-butyl-chloro-diphenyl-silane (3.0 g, 11 mmol). The mixture was stirred at room temperature for 4 h, washed with water, and the organic layer was concentrated, and the product was purified by column chromatography (50% EtOAc/$CH_2Cl_2$). Crystallization from nitromethane yielded 2.1 g (6.04 mmol, 66%) of **P1** as a colorless solid: **HR-ESI-MS** calculated for $C_{22}H_{26}NOSi^+$: 348.17837. Found: 348.17888 (1.48 ppm); **$^1$H NMR** ($CDCl_3$ 400 mHz): δ 8.56 (d, 2H, Py*H*, J = 5.2 Hz), 7.67 (d, 4H, Ar*H*, J = 7.2 Hz), 7.35-7.47 (m, 6H, Ar*H*), 7.28 (d, 2H, Py*H*, J = 5.2 Hz), 4.76 (s, 2H, C$H_2$), 1.12 (s, 9H, C$H_3$) ppm; **$^{13}$C NMR** ($CDCl_3$ 75 mHz): δ 150.0, 149.7, 135.5, 132.9, 129.9, 127.8, 120.6, 64.1, 26.8, 19.3 ppm.

**Viologen V2. A** solution of **3** (see Scheme S1; 91 mg, 0.18 mmol) and bromomethyl-cyclohexane (175 mg, 9.9 mmol) in DMF (5 mL) was stirred for 3 days at 95°C. After cooling, $Et_2O$ (3 mL) was added, and the precipitate was filtered off and washed with 20 mL of $Et_2O$. The resulting solid was dissolved in a minimal amount of a 1:1 (vol/vol) mixture of acetone and water followed by the addition of with $NH_4PF_6$ saturated water (10 mL). The resulting precipitate was filtered, washed with 40 mL of water, and then dried to obtain viologen **V2** as a white solid (50 mg, 0.061 mmol, 34 %). M.p.: >250°C.
**HR-ESI-MS** calculated for the sodium adduct of **V2** $C_{36}H_{52}F_6N_2NaOP_2^+$: 841.32609. Found: 841.32535 (-0.88 ppm); **$^1$H NMR** [400 MHz, $CD_3CN$:$CDCl_3$, 1:1 (vol/vol)]: δ8.94 (d, 2H, Bipy*H*, J = 7.2 Hz), 8.85 (d, 2H, Bipy*H*, J = 7.2 Hz), 8.42 (d, 2H, Bipy*H*, J = 3.6 Hz), 8.41 (d, 2H, Bipy*H*, J = 3.2 Hz), 7.02 (t, 1H, para-Ar*H*, J = 1.6 Hz), 6.73 (d, 2H, ortho-Ar*H*, J = 1.6 Hz), 4.67 (t, 2H, NC$H_2$, J = 7.6 Hz ), 4.48 (d, 2H, NC$H_2$, J = 7.6 Hz), 4.00 (t, 2H, OC$H_2$, J = 6.4 Hz), 2.12 (dd, 2H, C$H_2$, J = 7.6 Hz), 2.00 (m, 1H, C*H*), 1.86 (dd, 2H, C$H_2$, J = 7.6 Hz), 1.78 (m, 2H), 1.71 (m, 1H), 1.64 (m, 2H), 1.61 (m, 2H, C$H_2$), 1.30 (s, 18H, C$H_3$), 1.26 (m, 3H), 1.13 (m, 2H) ppm; **$^{13}$C NMR** [75 MHz, $CD_3CN$:$CDCl_3$, 1:1 (vol/vol)]: δ158.15, 151.72, 149.42, 145.13, 126.83, 126.72, 114.35, 108.32, 67.11, 66.57, 61.72, 39.04, 34.33, 30.61, 30.45, 28.94, 28.11, 25.19, 24.72, 22.12 ppm; Maldi-TOF MS: *m*/*z* 528.21 $(M-2PF_6)^+$.

**$^1$H NMR spectroscopy.** $^1$H NMR spectra of the formed pseudo-rotaxane complex between **Zn1** and **V2** is presented in Fig. S1. $^1$H NMR titration experiments of **Zn1**, and the viologen-receptor complexes, respectively, with **A1** are presented in Fig. S2.

**Fluorescence spectroscopy.** The excitation and emission slits were both set to 10 nm. All measurements were done in a $CHCl_3$/MeCN (1:1, v/v) solvent mixture at 298 K.

The rate and association constants as presented in Figs. 3-8 in the main text and Figs. S4 and S5 are included in Table S1. The Gibbs free energy ($\Delta G^o$) and the Gibbs free energy of activation ($\Delta G^{\neq}$) were derived from the measured rate and association constants and the resulting energy diagrams of the full cooperative binding circles are presented in Fig. S3.

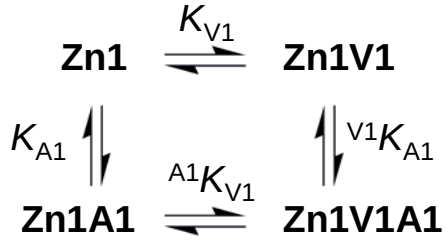
**Binding of A1 and A2 to reference porphyrin receptors.** In order to appreciate the relative magnitude of the zinc-nitrogen interaction between silyl-protected pyridine **A1** and pyridine **A2** in the used solvent mixture, the association constants of these guests to reference zinc porphyrins 5,10,15,20-tetrakis-(2-methoxy-phenyl)-Zn-porphyrin (**R1**) and 5,10,15,20-tetrakis-(3-methoxy-phenyl)-Zn-porphyrin (**R2**), respectively) were determined by UV-vis titrations. Association constants of $K_{R1\text{-}A2} = 1.4 \times 10^3$ M$^{-1}$ and $K_{R2\text{-}A2} = 1.0 \times 10^3$ M$^{-1}$ were obtained for the binding of **A2** with **R1** and **R2**, respectively, whereas values of $K_{R1\text{-}A1} = 2.1 \times 10^3$ M$^{-1}$ and $K_{R2\text{-}A1} = 1.8 \times 10^3$ M$^{-1}$ were obtained for the binding of **A1** with these reference zinc porphyrins. Based on these data, it can be assumed that the pyridine **A1** will have an association constant for the outside of **Zn1** which is roughly 1.6 times lower than that of **A2**, hence a value $K_{A2\text{-out}} = 80 \pm 15$ M$^{-1}$.

**X-Ray structure (Fig. 2).** Crystal structure data has been submitted to the Cambridge Crystallographic Data Center

**Derivation of the Equations.**

**(1) Eq. 1:** $$^{A1}K_{V1-app} = \frac{K_{V1} + {}^{A1}K_{V1} \cdot K_{A1} \cdot [A1]}{1 + K_{A1}[A1]}$$

The binding model for the combination **Zn1**, **A1** and **V1**, as in Fig. 1*A*:




With the individual association constants defined:

$$K_{V1} = \frac{[Zn1V1]}{[V1][Zn1]} \quad \textbf{[S1]}, \qquad K_{A1} = \frac{[Zn1A1]}{[A1][Zn1]} \quad \textbf{[S2]},$$

$${}^{V1}K_{A1} = \frac{[Zn1V1A1]}{[A1][Zn1V1]} \quad \textbf{[S3]}, \qquad {}^{A1}K_{V1} = \frac{[Zn1V1A1]}{[V1][Zn1A1]} \quad \textbf{[S4]},$$

and the cooperative thermodynamic effect describing the enhancement in complexation strength as a result of the binding of the other guest to the receptor:

$$Ce = \frac{{}^{A1}K_{V1}}{K_{V1}} = \frac{{}^{V1}K_{A1}}{K_{A1}} \quad \textbf{[S5]}.$$

The stability constant of the ternary complex is given:

$$K_{tern} = \frac{[Zn1V1A1]}{[Zn1][V1][A1]} = \frac{{}^{V1}K_{A1} \cdot K_{V1}[Zn1][V1][A1]}{[Zn1][V1][A1]} = Ce \cdot K_{A1} \cdot K_{V1}. \quad \textbf{[S6]}$$

While performing a titration experiment in which **V1** is added to a mixture of **Zn1** (~μM) and **A1** (excess compared to **Zn1**), the spectral changes of **Zn1** as a result of the addition of **V1** are monitored. This thus gives an apparent stability constant ${}^{A1}K_{V1\text{-app}}$ which is defined:

$${}^{A1}K_{V1-app} = \frac{[Zn1V1]+[Zn1V1A1]}{([Zn1]+[Zn1A1])\cdot[V1]} \quad \textbf{[S7]},$$

which can be rewritten with Eqs. **S1**, **S2**, and **S4** into:

$${}^{A1}K_{V1-app} = \frac{K_{V1}[Zn1][V1]+{}^{A1}K_{V1} \cdot K_{A1} \cdot [Zn1][A1][V1]}{([Zn1]+K_{A1}[Zn1][A1])\cdot[V1]}.$$

Rewriting gives:

$${}^{A1}K_{V1-app} = \frac{K_{V1}+{}^{A1}K_{V1} \cdot K_{A1} \cdot [A1]}{1+K_{A1}[A1]} \quad [\textbf{S8}] = \text{Eq. } \textbf{1}.$$

Because **A1** is present in excess compared to **Zn1**, the concentration of free **A1** ([**A1**]) remains virtually unchanged in the course of the titration experiment and can be assumed to be equal to the total concentration of **A1**: [**A1**] = $[\textbf{A1}]_o$. As a result, the apparent association constant ${}^{A1}K_{V1\text{-app}}$ remains constant in the course of the titration experiment with **V1**. Moreover, the fact that **A1** is present in excess also causes that the

experimentally obtained isotherm behaves virtually according to a 1:1 binding process: **X** + **V1** ⇌ **XV1** in which **X** = **Zn1**+ **Zn1A1** and **XV1** = **Zn1V1** + **Zn1V1A1**. This is the result of the fact that the relative ratios [**Zn1**]/[**ZnA1**] and [**ZnV1**]/[**ZnV1A1**] remain unaffected during the titration experiment (that is the fractional saturation of both **Zn1** and the complex **Zn1V1** with **A1** ($y_{\text{Zn1-A1}}$ and $y_{\text{Zn1V1-A1}}$) remain unaffected in the course of the experiment).

The experimental titration curves can therefore be fitted using a 1:1 binding isotherm from which one apparent association constant is obtained ${}^{\text{A1}}K_{\text{V1-app}}$ that depends on $K_{\text{V1}}$, $K_{\text{A1}}$, and [**A1**] (≈[**A**]$_o$) according to Eq. **S8** (Eq. **1** in the main text). Fitting such a binding curve to the full binding model will not be successful, because such a procedure relies on the deviations from the 1:1 binding behavior. These deviations are under the chosen experimental conditions so small that they can not be identified by fitting procedures covering the full binding model.

**(2) Eq. 3:** ${}^{\text{A1}}K_{\text{V1-app}} = K_{\text{V1}} \cdot \left(1 + y_{\text{Zn1-A1}} \{Ce - 1\}\right)$**, linear relation between** ${}^{\text{A1}}K_{\text{V1-app}}$ **and** $y_{\text{Zn-A1}}$**.**

The apparent association constant ${}^{\text{A1}}K_{\text{V1-app}}$ depends linearly on the fractional saturation of **Zn1** with **A1** ($y_{\text{Zn1-A1}}$).

The fractional saturation $y_{\text{Zn1-A1}}$ is defined:

$$y_{\text{Zn1-A1}} = \frac{K_{\text{A1}}[\text{A1}]}{1 + K_{\text{A1}}[\text{A1}]}. \qquad \textbf{[S9]}$$

Substitution of Eq. **S9** into Eq. **S8** gives:

$${}^{\text{A1}}K_{\text{V1-app}} = \frac{y_{\text{Zn1-A1}} \cdot K_{\text{V1}} \cdot \left(1 + Ce \cdot K_{\text{A1}} \cdot [\text{A1}]\right)}{K_{\text{A1}} \cdot [\text{A1}]},$$

rewriting,

$${}^{\text{A1}}K_{\text{V1-app}} = \frac{y_{\text{Zn1-A1}} \cdot K_{\text{V1}}}{K_{\text{A1}} \cdot [\text{A1}]} + y_{\text{Zn1-A1}} \cdot K_{\text{V1}} \cdot Ce = \left(\frac{1}{y_{\text{Zn1-A1}}} - 1\right) \cdot \left(y_{\text{Zn1-A1}} \cdot K_{\text{V1}}\right) + y_{\text{Zn1-A1}} \cdot K_{\text{V1}} \cdot Ce,$$

rewriting

$${}^{\text{A1}}K_{\text{V1-app}} = K_{\text{V1}} - y_{\text{Zn1-A1}} \cdot K_{\text{V1}} + y_{\text{Zn1-A1}} \cdot K_{\text{V1}} \cdot Ce,$$

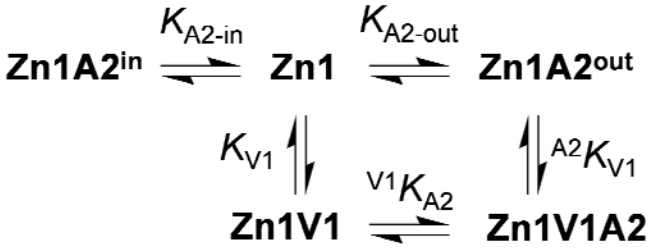
to give:

$${}^{A1}K_{V1-app} = K_{V1} \cdot \left(1 + y_{Zn1-A1}\{Ce - 1\}\right) \qquad \textbf{[S10]} = \text{Eq. } \textbf{3}.$$

There is thus a simple linear relation between the apparent association constant obtained for the binding between **V1** and **Zn1** in the presence of **A1**, and the fractional saturation of **Zn1** and **A1** (which remains of course constant during the titration experiment). For instance, when there is only 50% occupation of **Zn1** with **A1** (hence $y_{Zn1\text{-}A1} = 0.5$) the experimentally measured and calculated cooperative effect (*Ce*) for the binding of **V1** to **Zn1** in the presence of **A1** will only be half its actual value.

**(3) Eq. 4:** $${}^{A2}K_{V1-app} = \frac{K_{V1} + [A2] \cdot {}^{A2}K_{V1} \cdot K_{A2\text{-out}}}{\left(1 + [A2] \cdot K_{A2\text{-total}}\right)}$$

The binding model for the combination **Zn1**, **A2** and **V1**, as in Figure 1(b):




With the individual association constants defined:

$$K_{V1} = \frac{[Zn1V1]}{[V1][Zn1]} \qquad \textbf{[S1]}, \qquad K_{A2-in} = \frac{[Zn1A2^{in}]}{[A2][Zn1]} \qquad \textbf{[S11]},$$

$$K_{A2-out} = \frac{[Zn1A2^{out}]}{[A2][Zn1]} \qquad \textbf{[S12]}, \qquad {}^{V1}K_{A2} = \frac{[Zn1V1A2]}{[A2][Zn1V1]} \qquad \textbf{[S13]},$$

$${}^{A2}K_{V1} = \frac{[Zn1V1A2]}{[V1][Zn1A2^{out}]} \qquad \textbf{[S14]},$$

$$K_{A2-total} = K_{A2-in} + K_{A2-out} = \frac{[Zn1A2^{out}] + [Zn1A2^{in}]}{[A2][Zn1]} \qquad \textbf{[S15]},$$

$$Ce = \frac{{}^{A2}K_{V1}}{K_{V1}} = \frac{{}^{V1}K_{A2}}{K_{A2\text{-out}}} \; . \qquad \textbf{[S16]}$$

While performing a titration experiment in which **V1** is added to a mixture of **Zn1** (~μM) and **A2** (excess compared to **Zn1**), the spectral changes of **Zn1** as a result of the addition of **V1** are monitored. This thus gives an apparent stability constant ${}^{A2}K_{V1\text{-app}}$ which is defined:

$${}^{A2}K_{V1-app} = \frac{[Zn1V1]+[Zn1V1A2]}{[V1]\cdot\left([Zn1A2^{out}]+[Zn1A2^{in}]+[Zn1]\right)}, \qquad \textbf{[S17]}$$

rewriting with Eqs. **S1**, **S12**, and **S13**,

$${}^{A2}K_{V1-app} = \frac{[Zn1][V1]\cdot K_{V1}+[Zn1][A2][V1]\cdot {}^{A2}K_{V1}\cdot K_{A2\text{-out}}}{[V1]\cdot\left([Zn1][A2]K_{A2\text{-out}}+[Zn1]\cdot[A2]\cdot K_{A2\text{-in}}+Zn1\right)},$$

rewriting,

$${}^{A2}K_{V1-app} = \frac{K_{V1}+[A2]\cdot {}^{A2}K_{V1}\cdot K_{A2\text{-out}}}{\left([A2]K_{A2\text{-out}}+[A2]\cdot K_{A2\text{-in}}+1\right)},$$

Rewriting with Eq. **S15**,

$${}^{A2}K_{V1-app} = \frac{K_{V1}+[A2]\cdot {}^{A2}K_{V1}\cdot K_{A2\text{-out}}}{\left(1+[A2]\cdot K_{A2\text{-total}}\right)} \qquad \textbf{[S18]} = \text{Eq. } \textbf{4}.$$

The same assumptions can be made here as in the example with the combination **Zn1**, **A1**, and **V1**. Even though the binding model is significantly more complex as a result of the possibility of **A2** to coordinate both to the inside and outside of the cavity of **Zn1**, the curves can be simply analyzed with the help of straightforward 1:1 binding models. Needless to say that this method therefore has huge advantages over fitting programs covering the full binding model, which in this case would have to uncover 4 independent constants from a single experiment.

**(4) Eq. 5:** $${}^{A2}K_{V1\text{-app}} = K_{V1} + y_{Zn1-A2}\cdot\left(\frac{{}^{A2}K_{V1}\cdot K_{A2\text{-out}}}{K_{A2\text{-total}}} - K_{V1}\right)$$ **, linear relation between** ${}^{A2}K_{V1\text{-app}}$ **and** $y_{Zn\text{-}A2}$

The apparent association constant ${}^{A1}K_{V1\text{-app}}$ depends linearly on the fractional saturation of **Zn1** with **A2** ($y_{Zn1\text{-}A2}$).

The fractional saturation $y_{Zn1\text{-}A2}$ is defined:

$$y_{\text{Zn1–A2}} = \frac{K_{\text{A2–total}} \cdot [\text{A2}]}{1 + K_{\text{A2–total}} \cdot [\text{A2}]}. \qquad \textbf{[S19]}$$

Substitution of S19 into S18 gives:

$${}^{\text{A2}}K_{\text{V1-app}} = \frac{y_{\text{Zn1–A2}} \cdot \left(K_{\text{V1}} + [\text{A2}] \cdot {}^{\text{A2}}K_{\text{V1}} \cdot K_{\text{A2-out}}\right)}{[\text{A2}] \cdot K_{\text{A2-total}}},$$

rewriting,

$${}^{\text{A2}}K_{\text{V1-app}} = \frac{y_{\text{Zn1–A2}} \cdot K_{\text{V1}}}{[\text{A2}] \cdot K_{\text{A2-total}}} + \frac{y_{\text{Zn1–A2}} \cdot {}^{\text{A2}}K_{\text{V1}} \cdot K_{\text{A2-out}}}{K_{\text{A2-total}}},$$

rewriting,

$${}^{\text{A2}}K_{\text{V1-app}} = \left(\frac{1}{y_{\text{Zn1–A2}}} - 1\right) \cdot y_{\text{Zn1–A2}} \cdot K_{\text{V1}} + \frac{y_{\text{Zn1–A2}} \cdot {}^{\text{A2}}K_{\text{V1}} \cdot K_{\text{A2-out}}}{K_{\text{A2-total}}},$$

rewriting,

$${}^{\text{A2}}K_{\text{V1-app}} = K_{\text{V1}} - y_{\text{Zn1–A2}} \cdot K_{\text{V1}} + \frac{y_{\text{Zn1–A2}} \cdot {}^{\text{A2}}K_{\text{V1}} \cdot K_{\text{A2-out}}}{K_{\text{A2-total}}},$$

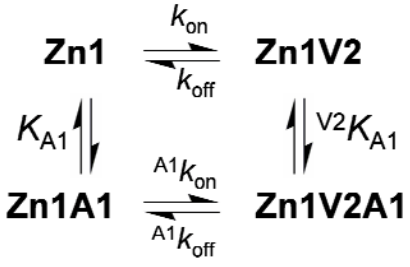
to give:

$${}^{\text{A2}}K_{\text{V1-app}} = K_{\text{V1}} + y_{\text{Zn1–A2}} \cdot \left(\frac{{}^{\text{A2}}K_{\text{V1}} \cdot K_{\text{A2-out}}}{K_{\text{A2-total}}} - K_{\text{V1}}\right). \qquad \textbf{[S20]} = \text{Eq. } \textbf{5}.$$

Hence the linear relation between ${}^{\text{A2}}K_{\text{V1-app}}$ and $y_{\text{Zn1-A2}}$.

**(5) Eq. 6: overall slippage rate equation.**

The binding model for the combination **Zn1**, **A1** and **V2**, as in Fig. 1*C*:




With the individual association constants defined:

$$K_{A1} = \frac{[Zn1A1]_{eq}}{[A1]_{eq}[Zn1]_{eq}} \quad \textbf{[S2]}, \qquad K_{V2} = \frac{k_{on}}{k_{off}} = \frac{[Zn1V2]_{eq}}{[V2]_{eq}[Zn1]_{eq}} \quad \textbf{[S21]},$$

$${}^{A1}K_{V2} = \frac{{}^{A1}k_{on}}{{}^{A1}k_{off}} = \frac{[Zn1V2A1]_{eq}}{[V2]_{eq}[Zn1A1]_{eq}} \quad \textbf{[S22]}, \qquad {}^{V2}K_{A1} = \frac{[Zn1V2A1]_{eq}}{[A1]_{eq}[Zn1V2]_{eq}} \quad \textbf{[S23]},$$

And the cooperative thermodynamic (*Ce*) and kinetic ($ce_{(on)}$ and $ce_{(off)}$) effects:

$$ce_{(on)} = \frac{{}^{A1}k_{on}}{k_{on}} \quad \textbf{[S24]}, \qquad ce_{(off)} = \frac{{}^{A1}k_{off}}{k_{off}} \quad \textbf{[S25]},$$

$$Ce = \frac{{}^{A1}K_{V2}}{K_{V2}} = \frac{{}^{V2}K_{A1}}{K_{A1}} = \frac{ce_{(on)}}{ce_{(off)}} \quad \textbf{[S26]}.$$

As for the combination **Zn1**, **A1**, **V1**, the same thermodynamic relations can be applied:

$${}^{A1}K_{V2-app} = \frac{K_{V2} + {}^{A1}K_{V2} \cdot K_{A1} \cdot [A1]}{1 + K_{A1}[A1]} \quad \textbf{[S27]},$$

$${}^{A1}K_{V2-app} = K_{V2} \cdot \left(1 + y_{Zn1-A1}\{Ce - 1\}\right) \quad \textbf{[S28]}.$$

The rate equation for the slippage between **Zn1** and **V2** in the presence of **A1**:

$$v = k_{on}[Zn1][V1] + {}^{A1}k_{on}[Zn1A1][V2] - k_{off}[Zn1V2] - {}^{A1}k_{off}[Zn1V2A1] \quad \textbf{[S29]}.$$

The ratios [**Zn1A1**]/[**Zn1**] and [**Zn1V2A1**]/[**Zn1V2**] will not change in the course of the experiment because the slippage over the cyclohexyl stopper is the slow rate determining process and **A1** is present in excess. Therefore, this experiment will display apparent 1:1 kinetic binding behavior according to a slippage reaction:

**X** + **V2** ⇌ **XV2**,

in which [**X**] = [**Zn1**] + [**Zn1A1**] = [$\mathbf{Zn1_{tot}}$], and [**XV2**] = [**Zn1V2**] + [**Zn1V2A1**] = [$\mathbf{Zn1V2_{tot}}$].

The overall rate equation can therefore be written:

$$v = {}^{A1}k_{on\text{-}app}[Zn1_{tot}][V1] - {}^{A1}k_{off\text{-}app}[Zn1V2_{tot}] = \frac{-d[Zn1_{tot}]}{dt} = \frac{-d[V2]}{dt} = \frac{d[Zn1V2]}{dt}$$

**[S30]** = Eq. **6**.

**(6) Apparent rate constants: Eqs. 7 and 8.**

The experimental slippage rate constants the combination **Zn1**, **A1** and **V2** displays apparent 1:1 kinetics with rate constants ${}^{A1}k_{\text{on-app}}$ and ${}^{A1}k_{\text{off-app}}$.

For the slippage (${}^{A1}k_{\text{on-app}}$):

$${}^{A1}k_{\text{on-app}}[\text{Zn1}_{\text{tot}}][\text{V1}] = k_{\text{on}}[\text{Zn1}][\text{V2}] + {}^{A1}k_{\text{on}}[\text{Zn1A1}][\text{V2}] \qquad \textbf{[S31]}$$

rewriting:

$${}^{A1}k_{\text{on-app}} = \frac{k_{\text{on}}[\text{Zn1}] + {}^{A1}k_{\text{on}}[\text{Zn1A1}]}{[\text{Zn1}] + [\text{Zn1A1}]}.$$

Rewriting

$${}^{A1}k_{\text{on-app}} = \frac{k_{\text{on}}[\text{Zn1}] + {}^{A1}k_{\text{on}} \cdot K_{\text{A1}}[\text{Zn1}][\text{A1}]}{[\text{Zn1}] + K_{\text{A1}}[\text{Zn1}][\text{A1}]}$$

to give

$${}^{A1}k_{\text{on-app}} = \frac{k_{\text{on}} + {}^{A1}k_{\text{on}} \cdot K_{\text{A1}}[\text{A1}]}{1 + K_{\text{A1}}[\text{A1}]} \qquad \textbf{[S32]} = \text{Eq. } \textbf{7}.$$

For the de-slippage (${}^{A1}k_{\text{off-app}}$):

$${}^{A1}k_{\text{off}-\text{app}}[\text{Zn1V2}_{\text{tot}}] = k_{\text{off}}[\text{Zn1V2}] + {}^{A1}k_{\text{off}}[\text{Zn1V2A1}] \qquad \textbf{[S33]},$$

Rewriting,

$${}^{A1}k_{\text{off-app}} = \frac{k_{\text{off}}[\text{Zn1V2}] + {}^{A1}k_{\text{off}}[\text{Zn1V2A1}]}{[\text{Zn1V2}] + [\text{Zn1V2A1}]}.$$

Rewriting,

$${}^{A1}k_{\text{off-app}} = \frac{k_{\text{off}}[\text{Zn1V2}] + {}^{A1}k_{\text{off}} \cdot {}^{V2}K_{\text{A1}}[\text{Zn1V2}][\text{A1}]}{[\text{Zn1V2}] + {}^{V2}K_{\text{A1}}[\text{Zn1V2}][\text{A1}]}$$

to give

$${}^{A1}k_{\text{off-app}} = \frac{k_{\text{off}} + {}^{A1}k_{\text{off}} \cdot {}^{V2}K_{\text{A1}}[\text{A1}]}{1 + {}^{V2}K_{\text{A1}}[\text{A1}]} \qquad \textbf{[S34]} = \text{Eq. } \textbf{8}.$$

**(7) Eqs. 9 and 10: linear relations of ${}^{A1}k_{\text{on-app}}$ with $y_{\text{Zn1-A1}}$ and of ${}^{A1}k_{\text{off-app}}$ with $y_{\text{Zn1V2-A1}}$**

Linear relation of ${}^{A1}k_{\text{on-app}}$ with $y_{\text{Zn1-A1}}$.

The fractional saturation of **Zn1** with **A1**, $y_{\text{Zn1-A1}}$:

$$y_{\text{Zn1-A1}} = \frac{K_{\text{A1}}[\text{A1}]}{1 + K_{\text{A1}}[\text{A1}]} \qquad \textbf{[S9]}.$$

Substitution of Eqs. **S9** and **S24** into Eq. **S32**:

$${}^{A1}k_{\text{on-app}} = \frac{y_{\text{Zn1-A1}} \cdot k_{\text{on}} \cdot \left(1 + ce_{\text{(on)}} \cdot K_{\text{A1}} \cdot [\text{A1}]\right)}{K_{\text{A1}} \cdot [\text{A1}]}$$

To give eventually as derived above for ${}^{A1}K_{\text{V1}}$:

$${}^{A1}k_{\text{on-app}} = k_{\text{on}} \cdot \left\{1 + y_{\text{Zn1-A1}} \cdot (ce_{\text{(on)}} - 1)\right\} \qquad \textbf{[S35]} = \text{Eq. } \textbf{9}.$$

Linear relation of ${}^{A1}k_{\text{off-app}}$ with $y_{\text{Zn1V2-A1}}$:

The fractional saturation of pseudorotaxane complex **Zn1V2** with **A1**, $y_{\text{Zn1V2-A1}}$:

$$y_{\text{Zn1V2-A1}} = \frac{{}^{V2}K_{\text{A1}}[\text{A1}]}{1 + {}^{V2}K_{\text{A1}}[\text{A1}]}. \qquad \textbf{[S36]}$$

Substitution of Eqs. **S36** and **S25** into Eq. **S34**:

$${}^{A1}k_{\text{off-app}} = \frac{y_{\text{Zn1V2-A1}} \cdot k_{\text{off}} \left(1 + ce_{\text{(off)}} \cdot {}^{V2}K_{\text{A1}}[\text{A1}]\right)}{{}^{V2}K_{\text{A1}}[\text{A1}]}.$$

Rewriting,

$${}^{A1}k_{\text{off-app}} = \frac{y_{\text{Zn1V2-A1}} \cdot k_{\text{off}}}{{}^{V2}K_{\text{A1}}[\text{A1}]} + ce_{\text{(off)}} \cdot y_{\text{Zn1V2-A1}} \cdot k_{\text{off}}.$$

Rewriting,

$${}^{A1}k_{\text{off-app}} = \left(y_{\text{Zn1V2-A1}} \cdot k_{\text{off}}\right) \cdot \left(\frac{1}{y_{\text{Zn1V2-A1}}} - 1\right) + ce_{\text{(off)}} \cdot y_{\text{Zn1V2-A1}} \cdot k_{\text{off}}.$$

Rewriting,

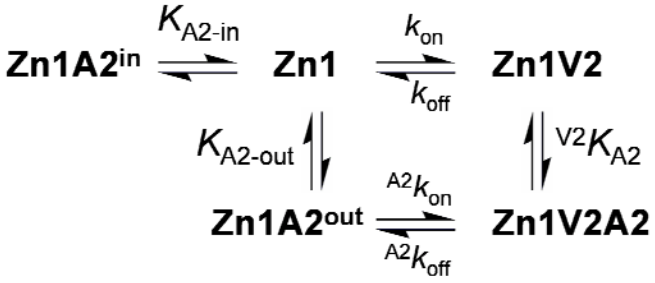
$${}^{A1}k_{\text{off-app}} = k_{\text{off}} - y_{\text{Zn1V2-A1}} \cdot k_{\text{off}} + ce_{\text{(off)}} \cdot y_{\text{Zn1V2-A1}} \cdot k_{\text{off}},$$

to give:

$${}^{A1}k_{\text{off-app}} = k_{\text{off}} \left(1 + y_{\text{Zn1V2-A1}} \left\{ce_{\text{(off)}} - 1\right\}\right) \textbf{ [S37]} = \text{Eq. } \textbf{10}.$$

**(8) Eqs. 11 and 12: Slippage rate constants in the presence of A2**

The binding model for the combination **Zn1**, **A2** and **V2**, as in Fig. 1*D*:




With the individual association constants defined:

$$K_{\mathrm{V2}} = \frac{k_{\mathrm{on}}}{k_{\mathrm{off}}} = \frac{[\mathrm{Zn1V2}]_{\mathrm{eq}}}{[\mathrm{V2}]_{\mathrm{eq}}[\mathrm{Zn1}]_{\mathrm{eq}}} \qquad \textbf{[S21]},$$

$$K_{\mathrm{A2-in}} = \frac{[\mathrm{Zn1A2^{in}}]}{[\mathrm{A2}][\mathrm{Zn1}]} \qquad \textbf{[S11]},$$

$$K_{\mathrm{A2-out}} = \frac{[\mathrm{Zn1A2^{out}}]}{[\mathrm{A2}][\mathrm{Zn1}]} \qquad \textbf{[S12]},$$

$${}^{\mathrm{V2}}K_{\mathrm{A2}} = \frac{[\mathrm{Zn1V2A2}]_{\mathrm{eq}}}{[\mathrm{A2}]_{\mathrm{eq}}[\mathrm{Zn1V2}]_{\mathrm{eq}}} \qquad \textbf{[S38]},$$

$${}^{\mathrm{A2}}K_{\mathrm{V2}} = \frac{{}^{\mathrm{A2}}k_{\mathrm{on}}}{{}^{\mathrm{A2}}k_{\mathrm{off}}} = \frac{[\mathrm{Zn1V2A2}]_{\mathrm{eq}}}{[\mathrm{V2}]_{\mathrm{eq}}[\mathrm{Zn1A2}]_{\mathrm{eq}}} \qquad \textbf{[S39]},$$

$$K_{\mathrm{A2-total}} = K_{\mathrm{A2-in}} + K_{\mathrm{A2-out}} = \frac{[\mathrm{Zn1A2^{out}}] + [\mathrm{Zn1A2^{in}}]}{[\mathrm{A2}][\mathrm{Zn1}]} \qquad \textbf{[S15]},$$

and the cooperative thermodynamic (*Ce*) and kinetic ($ce_{(\mathrm{on})}$ and $ce_{(\mathrm{off})}$) effects:

$$ce_{(\mathrm{on})} = \frac{{}^{\mathrm{A2}}k_{\mathrm{on}}}{k_{\mathrm{on}}} \qquad \textbf{[S40]},$$

$$ce_{(\mathrm{off})} = \frac{{}^{\mathrm{A2}}k_{\mathrm{off}}}{k_{\mathrm{off}}} \qquad \textbf{[S41]},$$

$$Ce = \frac{{}^{\mathrm{A2}}K_{\mathrm{V2}}}{K_{\mathrm{V2}}} = \frac{{}^{\mathrm{V2}}K_{\mathrm{A2}}}{K_{\mathrm{A2}}} = \frac{ce_{(\mathrm{on})}}{ce_{(\mathrm{off})}} \qquad \textbf{[S42]}.$$

As for the combination **Zn1**, **A2**, **V1**, the same thermodynamic relations can be applied:

$${}^{\mathrm{A2}}K_{\mathrm{V2-app}} = \frac{K_{\mathrm{V2}} + [\mathrm{A2}] \cdot {}^{\mathrm{A2}}K_{\mathrm{V2}} \cdot K_{\mathrm{A2\text{-}out}}}{\left(1 + [\mathrm{A2}] \cdot K_{\mathrm{A2\text{-}total}}\right)} \qquad \textbf{[S43]},$$

and the linear relation with respect to the fractional saturation of **Zn1** with **A2** ($y_{\mathrm{Zn1\text{-}A2}}$, Eq. **S19**):

$${}^{\mathrm{A2}}K_{\mathrm{V2\text{-}app}} = K_{\mathrm{V2}} + y_{\mathrm{Zn1-A2}} \cdot \left( \frac{{}^{\mathrm{A2}}K_{\mathrm{V2}} \cdot K_{\mathrm{A2\text{-}out}}}{K_{\mathrm{A2\text{-}total}}} - K_{\mathrm{V2}} \right) \qquad \textbf{[S44]}.$$

The apparent rate constants ${}^{\mathrm{A2}}k_{\mathrm{on}}$ and ${}^{\mathrm{A2}}k_{\mathrm{off}}$ can be simply derived from the rate equation:

$$v = {}^{A2}k_{on}[Zn1A2][V2] + k_{on}[Zn1][V2] - {}^{A2}k_{off}[Zn1V2A2] - k_{off}[Zn1V2] \qquad \textbf{[S45]},$$

the following relation can be obtained:

$${}^{A2}k_{on-app}\left([Zn] + [Zn1A2^{in}] + [Zn1A2^{out}]\right)\cdot[V2] = k_{on}[Zn1][V2] + {}^{A2}k_{on}[ZnA2^{out}][V2],$$

rewriting,

$${}^{A2}k_{on-app} = \frac{k_{on}[Zn1] + {}^{A2}k_{on}[ZnA2^{out}]}{[Zn] + [Zn1A2^{in}] + [Zn1A2^{out}]}.$$

Substitution with Eqs. **S11** and **S12** gives:

$${}^{A2}k_{on-app} = \frac{k_{on}[Zn1] + {}^{A2}k_{on} \cdot K_{A2-out}[Zn][A2]}{[Zn] + K_{A2-in}[Zn1][A2] + K_{A2-out}[Zn][A2]}.$$

Substitution with Eq. **S15** gives

$${}^{A2}k_{on-app} = \frac{k_{on} + {}^{A2}k_{on} \cdot K_{A2-out}[A2]}{1 + K_{A2-total} \cdot [A2]} \qquad \textbf{[S46]} = \text{Eq. } \textbf{11}.$$

The following de-slippage relation can be obtained from Eq. **S45**:

$${}^{A2}k_{off-app} \cdot \left([Zn1V2] + [Zn1V2A2]\right) = k_{off}[Zn1V2] + {}^{A2}k_{off}[Zn1V2A2],$$

which rewrites into:

$${}^{A2}k_{off-app} = \frac{k_{off}[Zn1V2] + {}^{A2}k_{off}[Zn1V2A2]}{[Zn1V2] + [Zn1V2A2]}.$$

Substitution with equation S38 gives:

$${}^{A2}k_{off-app} = \frac{k_{off}[Zn1V2] + {}^{A2}k_{off} \cdot {}^{V2}K_{A2}[Zn1V2][A2]}{[Zn1V2] + {}^{V2}K_{A2}[Zn1V2][A2]},$$

which becomes:

$${}^{A2}k_{off-app} = \frac{k_{off} + {}^{A2}k_{off} \cdot {}^{V2}K_{A2}[A2]}{1 + {}^{V2}K_{A2}[A2]} \qquad \textbf{[S47]} = \text{Eq. } \textbf{12}.$$

${}^{A2}k_{on\text{-}app}$ depends linearly on the fractional saturation of **Zn1** with **A2** ($y_{Zn1\text{-}A2}$):

$${}^{A2}k_{on-app} = k_{on} + y_{Zn1A2} \cdot \left( \frac{K_{A2-out} \cdot {}^{A2}k_{on}}{K_{A2-total}} - k_{on} \right) \textbf{[S48]}.$$

${}^{A2}k_{off\text{-}app}$ depends linearly on the fractional saturation of the pseudorotaxane complex **Zn1V2** with **A2** ($y_{Zn1V2\text{-}A2}$).

$$y_{Zn1V2-A2} = \frac{{}^{V2}K_{A2}[A2]}{1 + {}^{V2}K_{A2}[A2]} \qquad \textbf{[S49]}$$

the linear relation:

$${}^{A2}k_{\text{off-app}} = k_{\text{off}}\left(1 + y_{\text{Zn1V2-A2}}\left\{ce_{(\text{off})} - 1\right\}\right)$$ **[S50]**.

**(9) The symmetry op the model:**

In the main text, it is written that Eq. **1** (for the combination **Zn1**, **A1**, and **V2**) is obtained when Eq. **7** is divided by Eq. **8**. The derivation is as follows:

$${}^{A1}K_{\text{V2-app}} = \frac{K_{\text{V2}} + [\text{A1}]\cdot K_{\text{A1}}\cdot {}^{A1}K_{\text{V2}}}{1 + [\text{A1}]\cdot K_{\text{A1}}} = \frac{{}^{A1}k_{\text{on}}}{{}^{A1}k_{\text{off}}},$$

$$\frac{{}^{A1}k_{\text{on}}}{{}^{A1}k_{\text{off}}} = \left(\frac{k_{\text{on}} + {}^{A1}k_{\text{on}}\cdot K_{\text{A1}}\cdot[\text{A1}]}{1 + K_{\text{A1}}\cdot[\text{A1}]}\right) \Big/ \left(\frac{k_{\text{off}} + {}^{A1}k_{\text{off}}\cdot {}^{V2}K_{\text{A1}}\cdot[\text{A1}]}{1 + {}^{V2}K_{\text{A1}}\cdot[\text{A1}]}\right)$$

rRewrites into:

$$\frac{{}^{A1}k_{\text{on}}}{{}^{A1}k_{\text{off}}} = \left(\frac{k_{\text{on}} + {}^{A1}k_{\text{on}}\cdot K_{\text{A1}}\cdot[\text{A1}]}{1 + K_{\text{A1}}\cdot[\text{A1}]}\right)\cdot\left(\frac{1 + {}^{V2}K_{\text{A1}}\cdot[\text{A1}]}{k_{\text{off}} + {}^{A1}k_{\text{off}}\cdot {}^{V2}K_{\text{A1}}\cdot[\text{A1}]}\right).$$

Rewriting

$$\frac{{}^{A1}k_{\text{on}}}{{}^{A1}k_{\text{off}}} = \left(\frac{k_{\text{on}} + ce_{(\text{on})}\cdot k_{\text{on}}\cdot K_{\text{A1}}\cdot[\text{A1}]}{1 + K_{\text{A1}}\cdot[\text{A1}]}\right)\cdot\left(\frac{1 + Ce\cdot K_{\text{A1}}\cdot[\text{A1}]}{k_{\text{off}} + k_{\text{off}}\cdot ce_{(\text{off})}\cdot Ce\cdot K_{\text{A1}}\cdot[\text{A1}]}\right)$$

rewriting

$$\frac{{}^{A1}k_{\text{on}}}{{}^{A1}k_{\text{off}}} = \frac{\left(k_{\text{on}} + ce_{(\text{on})}\cdot k_{\text{on}}\cdot K_{\text{A1}}\cdot[\text{A1}]\right)\cdot\left(1 + Ce\cdot K_{\text{A1}}\cdot[\text{A1}]\right)}{\left(1 + K_{\text{A1}}\cdot[\text{A1}]\right)\cdot\left(k_{\text{off}} + k_{\text{off}}\cdot ce_{(\text{off})}\cdot Ce\cdot K_{\text{A1}}\cdot[\text{A1}]\right)}$$

rewriting

$$\frac{{}^{A1}k_{\text{on}}}{{}^{A1}k_{\text{off}}} = \frac{\left(k_{\text{off}}\cdot K_{\text{V2}} + ce_{(\text{off})}\cdot Ce\cdot k_{\text{off}}\cdot K_{\text{V2}}\cdot K_{\text{A1}}\cdot[\text{A1}]\right)\cdot\left(1 + Ce\cdot K_{\text{A1}}\cdot[\text{A1}]\right)}{\left(1 + K_{\text{A1}}\cdot[\text{A1}]\right)\cdot\left(k_{\text{off}} + k_{\text{off}}\cdot ce_{(\text{off})}\cdot Ce\cdot K_{\text{A1}}\cdot[\text{A1}]\right)}$$

rewriting

$$\frac{{}^{A1}k_{\text{on}}}{{}^{A1}k_{\text{off}}} = \frac{K_{\text{V2}}\cdot\left(k_{\text{off}} + ce_{(\text{off})}\cdot Ce\cdot k_{\text{off}}\cdot K_{\text{A1}}\cdot[\text{A1}]\right)\cdot\left(1 + Ce\cdot K_{\text{A1}}\cdot[\text{A1}]\right)}{\left(1 + K_{\text{A1}}\cdot[\text{A1}]\right)\cdot\left(k_{\text{off}} + k_{\text{off}}\cdot ce_{(\text{off})}\cdot Ce\cdot K_{\text{A1}}\cdot[\text{A1}]\right)}$$

eliminating,

$$\frac{^{A1}k_{on}}{^{A1}k_{off}} = \frac{K_{V2} \cdot (1 + Ce \cdot K_{A1} \cdot [A1])}{1 + K_{A1} \cdot [A1]},$$

rewriting:

$$\frac{^{A1}k_{on}}{^{A1}k_{off}} = \frac{K_{V2} + K_{A1} \cdot {}^{A1}K_{V2} \cdot [A1]}{1 + K_{A1} \cdot [A1]} = {}^{A1}K_{V2-app}$$

**(10) The general effect of competition (Eq. 13)**

Imagine a titration experiment of a guest (G) to a receptor (R) in the presence of any competing species (X) present in excess (for instance solvent, salt, acid or base).

$RX \rightleftharpoons R + X + G \rightleftharpoons RG$

in which:

$$K_X = \frac{[RX]}{[R][X]} \qquad \textbf{[S51]}, \qquad K_G = \frac{[RG]}{[R][G]} \qquad \textbf{[S52]}.$$

While monitoring the spectral changes to the receptor as a result of addition of the guest G the obtained association constant will have an apparent value depending on the magnitude of the competing species X.

$$K_{G-app} = \frac{[RG]}{([R] + [RX]) \cdot [G]} \qquad \textbf{[S53]},$$

Substituting Eqs. **S51** and **S52** into Eq. **S53** gives:

$$K_{G-app} = \frac{[R][G]K_G}{([R] + [R][X]K_X) \cdot [G]},$$

which rewrites into:

$$K_{G-app} = \frac{K_G}{1 + K_X \cdot [X]} \qquad \textbf{[S54]} = \text{Eq. } \textbf{13}.$$

This equation is added to the text to stress that association constants measured in solution are intrinsically apparent, because the solvent always has some interactions with the receptor (and with the guests). As a result of the solvents high concentration, these interactions will inevitably effect the outcome of any obtained binding constant. Although binding events always behave according to a 1:1 binding isotherms (as long as 1:1 species are formed exclusively, or the conditions are obeyed as described in the main text), the calculated value for the stability constant is still apparent and depends per

definition on the medium the measurement was performed in. This is therefore a powerful reminder that the free binding energy calculated from a titration experiment in solution never concerns the interactions between receptor and guest only.

1. Elemans JAAW, Bijsterveld EJA, Rowan AE, Nolte RJM (2007) Manganese porphyrin hosts as epoxidation catalysts--Activity and stability control by .axial ligand effects. *Eur J Org Chem* 751-757.

2. Elemans JAAW, et al. (1999) Porphyrin clips derived from diphenylglycoluril. Synthesis, conformational analysis, and binding properties. *J Org Chem* 64:7009-7016.

3. Coumans RGE, Elemans JAAW, Nolte RJE, Rowan AE (2006) Processive enzyme mimic: Kinetics and thermodynamics of the threading and sliding process. *Proc Natl Acad Sci USA* 103:19647-19651.