Supporting information for

Self-assembly between dicarboxylate ions and binuclear europium complexes: moving to water—pH dependence and effects of buffers

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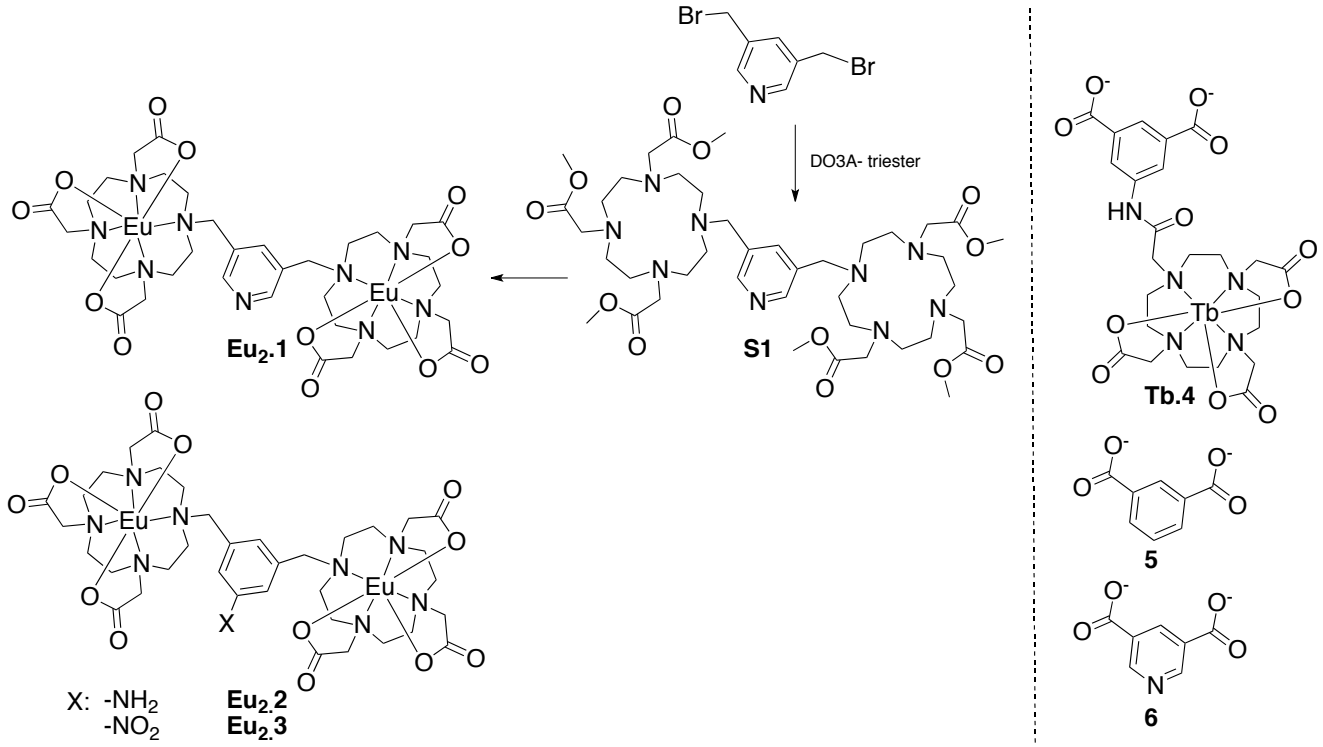
Contents

Molecular structures and Synthesis



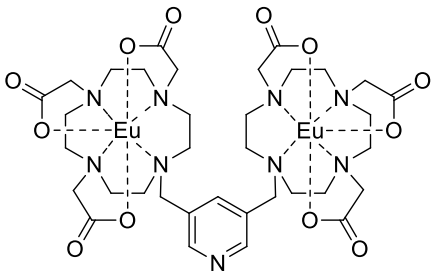
α,α'-bis(DO3A)-3,5-dimethylpyridine *tert*-butyl hexa ester (S1)

1,4,7-Tris(*tert*-butoxycarbonylmethyl)-1,4,7,10-tetraazacyclododecane (0.234 g, 0.455 mmol) and 3,5-bis(chloromethyl)pyridine[1] (0.040 g, 0.227 mmol) were dissolved in dry CH_3CN (10 mL) and Cs_2CO_3 (0.163 g, 0.500 mmol) was added. The mixture was heated at reflux under an atmosphere of N_2 for 60 hours, before being cooled to room temperature and filtered. After concentration of the filtrate on a rotary evaporator, the oily brown residue was dissolved in CH_2Cl_2 (25 mL) and the solution was washed with sat. $NaCl_{(aq)}$ (3 x 20 mL), dried over $MgSO_4$ and concentrated on a rotary evaporator. Purification of the residue by column chromatography (CH_2Cl_2:MeOH 98:2 graded to 85:15) afforded the title compound as a glassy yellow solid (0.102 g, 40%). Mp = 119–121 °C; δ_H(500 MHz, DMSO-d_6, 398 K): 1.43 (s, 36 H, ^{t}Bu-CH_3); 1.45 (s, 18 H, ^{t}Bu-CH_3), 2.66–2.69 (m, 8 H, NCH_2), 2.78–2.81 (m, 24 H, NCH_2), 3.17 (s, 8 H, NCH_2CO$_2$C(CH$_3$)$_3$), 3.25 (s, 4 H, NCH_2CO$_2$(CH$_3$)$_3$), 3.64 (s, 4 H, NCH_2Ar), 7.67 (t, ^4J = 1.5 Hz, 1 H, py-Ar*H*), 8.44 (d, ^4J = 1.5 Hz, 2 H, py-Ar*H*); δ_C(75 MHz, DMSO-d_6, 293 K): 27.6, 27.7 (CCH_3), 49.1 (br), 54.3, 55.6, 55.8 (NCH_2), 81.6, 81.8 (*C*CH$_3$), 130.1, 140.5, 150.1 (Ar), 172.8 (*C*O); ESMS: *m/z* 577.9 {M + Na + H}$^{2+}$, 588.9 {M + 2Na}$^{2+}$, 1132.8 {M + H}$^+$, 1154.8 {M + Na}$^+$; HRMS (ES): *m/z* 588.8821 ({M + 2Na}$^{2+}$. 0.5$C_{59}H_{105}N_9NaO_{12}$ requires 588.8834).

α,α'-bis(DO3A)-3,5-dimethylpyridine hexaaccid (H_6.1)

The hexaester **3** (0.090 g, 0.079 mmol) was dissolved in CH_2Cl_2 (5 mL) and trifluoroacetic acid (5 mL) was added dropwise. The solution was stirred at room temperature under an atmosphere of N_2 for 48 hours, before removal of the solvents on a rotary evaporator. The residue was dissolved in MeOH (1 mL) and Et_2O (20 mL) was added. The resulting precipitate was collected by filtration, washed with Et_2O (4 x 5 mL) and dried under vacuum to give **H_6.1** as as a trifluoroacetic acid adduct (yellow solid, 0.090 g). Mp = 210–214 °C; δ_H(500 MHz, DMSO-d_6, 393 K): 2.88–2.90 (m, 8 H, NCH_2), 2.98–3.02 (m, 16 H, NCH_2), 3.07–3.09 (m, 8 H, NCH_2), 3.47 (s, 8 H, NCH_2CO$_2$H), 3.54 (s, 4 H, NCH_2CO$_2$H), 3.99 (s, 4 H, NCH_2Ar), 8.03 (t, ^4J = 1.9 Hz, 1 H, py-Ar*H*), 8.54 (d, ^4J = 1.9 Hz, 2 H, py-Ar*H*); δ_C(126 MHz, DMSO-d_6, 293 K): 48.7, 49.7, 50.4, 54.3 (br, N*C*H$_2$), 117.3 (q, ^1J = 301 Hz, *C*F$_3$CO$_2$H), 130.9, 140.8, 150.4 (br, Ar), 158.1 (CF$_3$*C*O$_2$H), 170.1, 171.5 (br, *C*O); δ_F(282 MHz, DMSO-d_6): −74 (s); MALDI-TOF MS: *m/z* 796.6 {M}$^+$.

Eu_2.(α, α'-bis(DO3A)-3,5-dimethylpyridine) (Eu_2.1)



Pyridine-3,5-bisDO3A hexaacid (20 mg, 0.016 mmol) was dissolved in MeOH (2mL) and the pH adjusted to 5 (with dilute NaOH or HCl), if required. Europium triflate (19.14 mg, 0.032 mg) was added and the pH adjusted to 5, if required. This was left for 15 minutes and the pH adjusted to 5 again, if required. The ligand is more soluble at lower pH and the solution becomes a suspension at higher pH values, for example pH 7. The solution was heated at reflux under nitrogen for 48 hours. The reaction mixture was cooled to room temperature and the solvent removed under reduced pressure. Water was added to dissolve the suspended solid and 0.1 M NaOH added until the pH reached a value of 10. The mixture was centrifuged for 6 minutes and then filtered through an acrodisc. The basic solution was then concentrated under reduced pressure. Yield:

δ_H/ppm (300 MHz, D_2O) = 30.67, 23.87, 12.92, 12.28, 10.92, 8.83, 7.65, 7.58, 3.65, 2.34, 1.90, -3.98, -5.98, -8.69, -9.88, -11.86, -12.22, -13.03, -15.12, -16.49, -17.76

MALDITOF+ (*m/z*) predicted:1092.2, 1094.2, 1096.2, 1097.2 ($[M + H]^+$); measured: 1092.5, 1093.5, 1095.5, 1096.5, 1097.5 ($[M + H]^+$), 1116 ($[M + Na]^+$).

References:

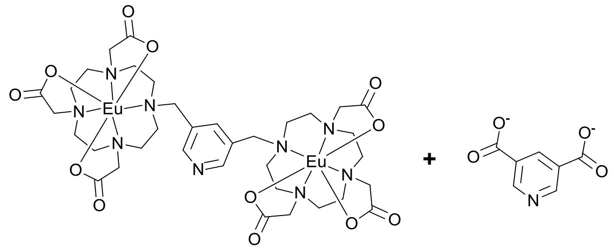
1. M.-C. Lagunas, R. A. Gossage, W. J. J. Smeets, A. L. Spek and G. van Koten, *Eur. J. Inorg. Chem.*, 1998, **1998**, 163-168.

Electronic Supplementary Material (ESI) for Dalton Transactions

Titration curves, Spectra and Fitting

Eu_2.1:6 – TRIS pH = 9

Host and Guest



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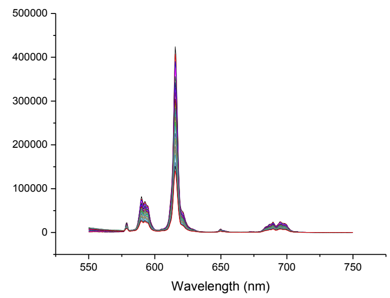
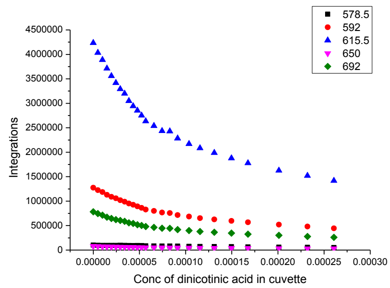


Solvent: TRIS buffer pH = 9

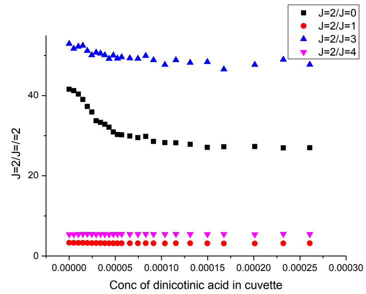
Quenching? Yes

Stern-Volmer Linear? No

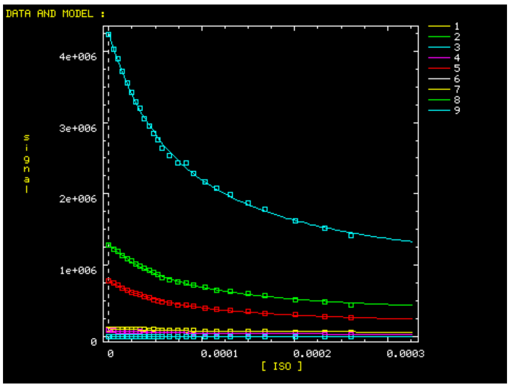
Binding curve Intensity



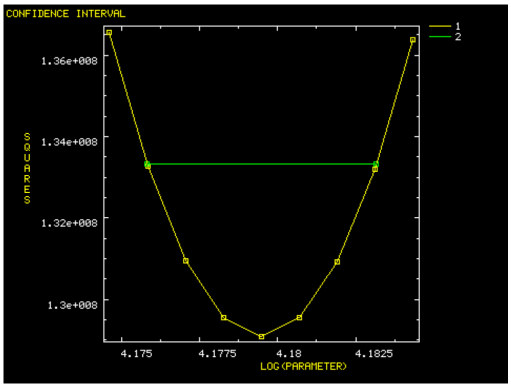
Binding curve I(ΔJ=2)/I(ΔJ=X)



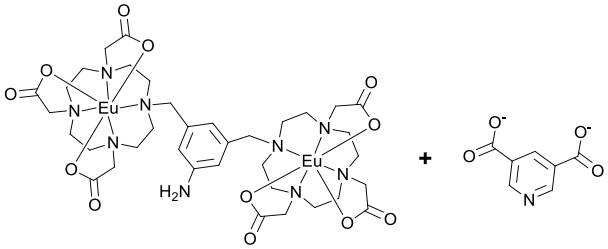
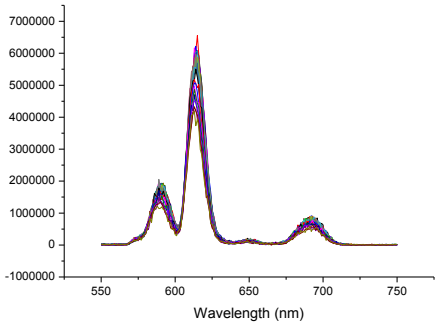
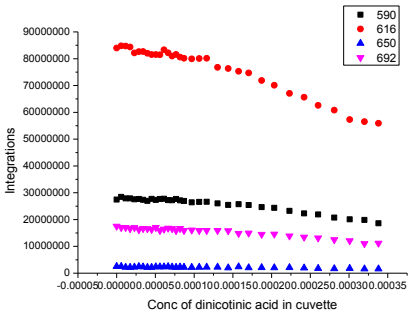
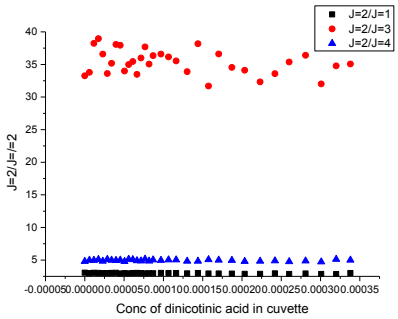
Binding curve Fit



Confidence interval of K

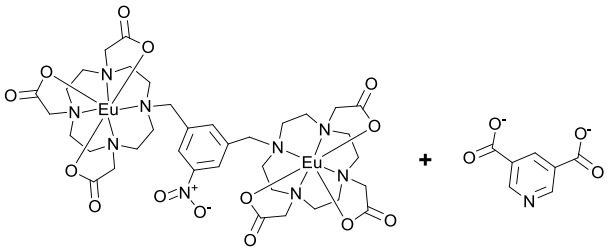


Eu_2.2:6 – TRIS pH = 9

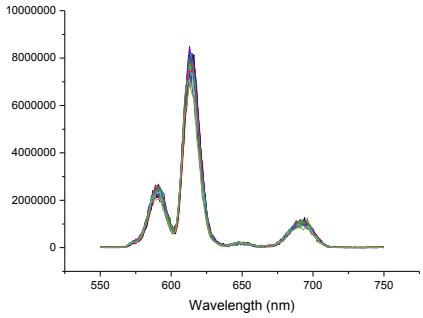
Host and Guest		Spectra	
Solvent	TRIS buffer pH = 9		
Quenching?	Yes		
Stern-Volmer Linear?	Yes, for the decrease in intensity following the flat start		
Binding curve Intensity		Binding curve I(ΔJ=2)/I(ΔJ=X)	
Binding curve Fit	-	Confidence interval of K	-

Eu_2.3:6 – TRIS pH = 9

Host and Guest

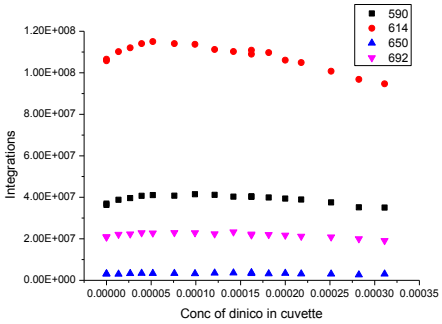


Spectra

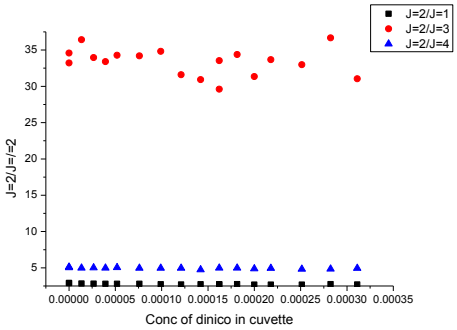


Solvent	TRIS buffer pH = 9
Quenching?	Yes
Stern-Volmer Linear?	Yes, for the decrease in intensity

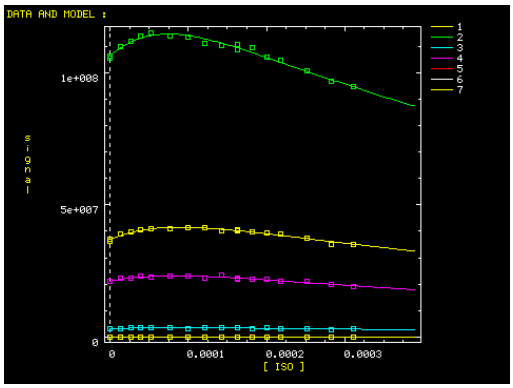
Binding curve Intensity



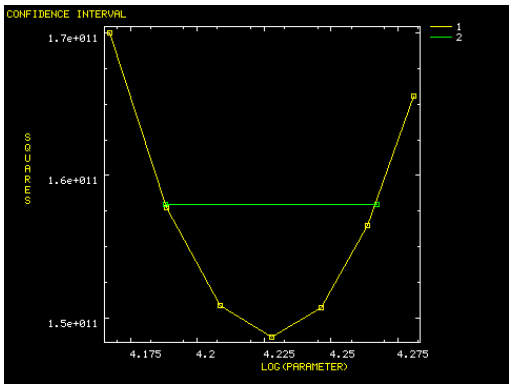
Binding curve I(ΔJ=2)/I(ΔJ=X)



Binding curve Fit

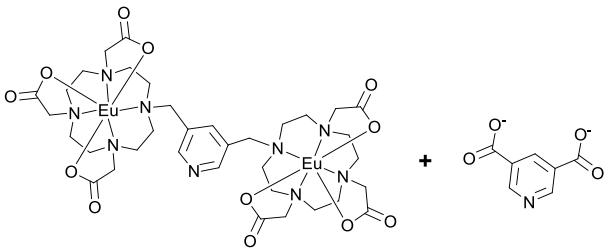


Confidence interval of K



Eu_2.1:6 – TRIS pH = 7

Host and Guest



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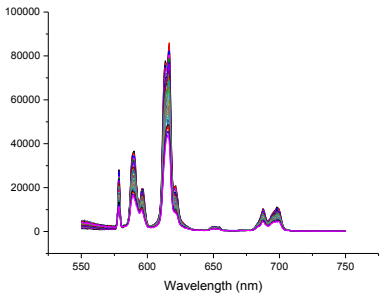
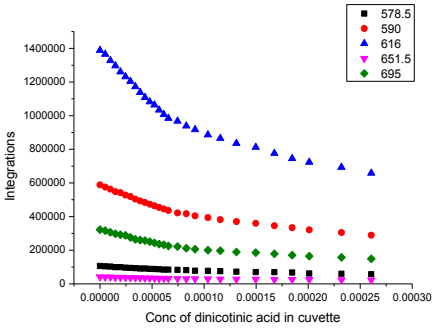
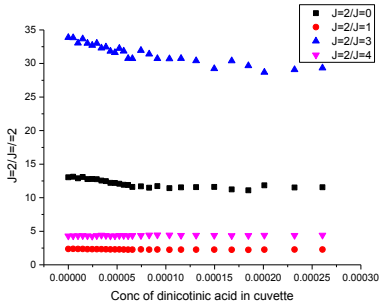


Solvent	TRIS buffer pH = 7
Quenching?	Yes
Stern-Volmer Linear?	No

Binding curve Intensity



Binding curve I(ΔJ=2)/I(ΔJ=X)



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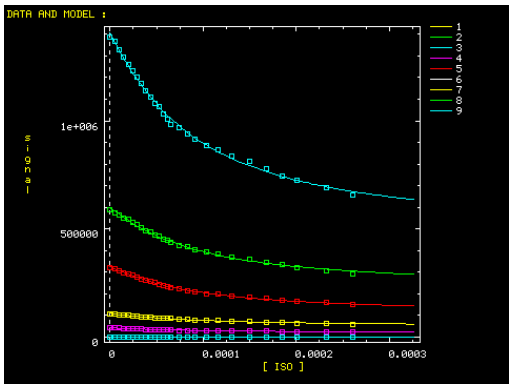

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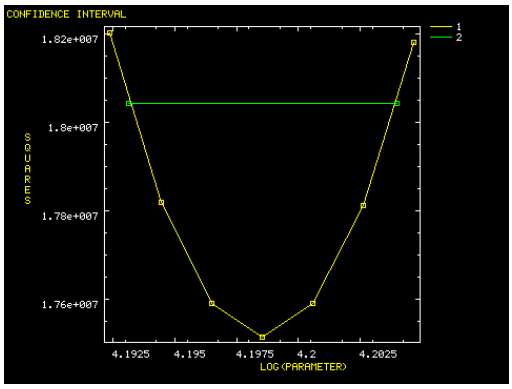

Eu_2.1:6 – TRIS pH = 8

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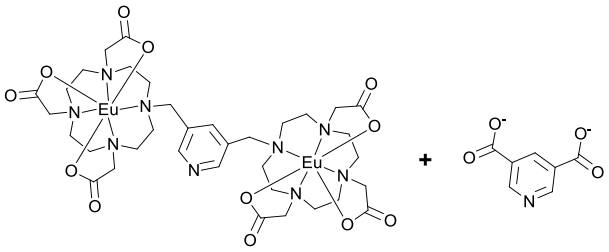

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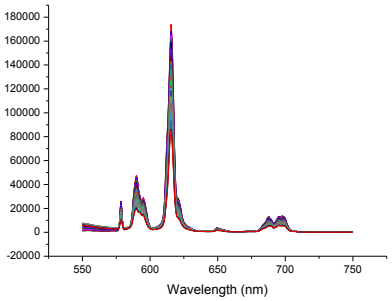
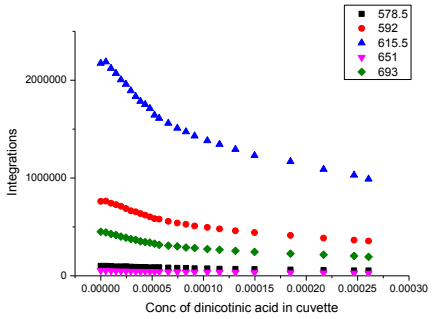
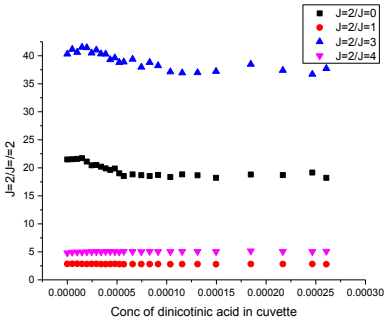


Solvent	TRIS buffer pH = 8
Quenching?	Yes
Stern-Volmer Linear?	No

Binding curve Intensity



Binding curve I(ΔJ=2)/I(ΔJ=X)



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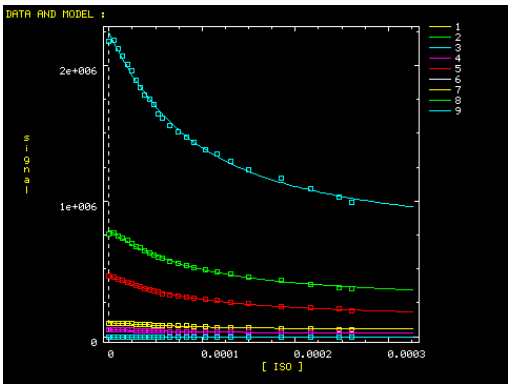

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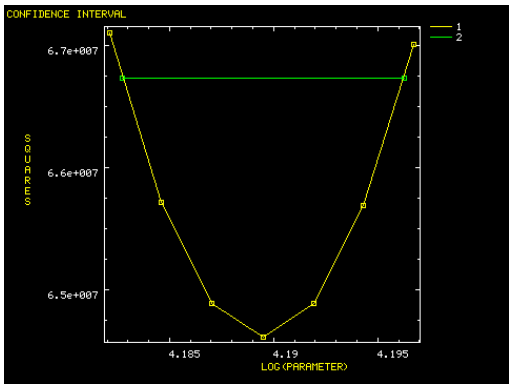

Eu_2.1:6 – TRIS pH = 10.5

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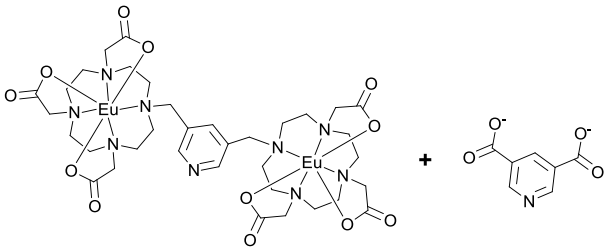

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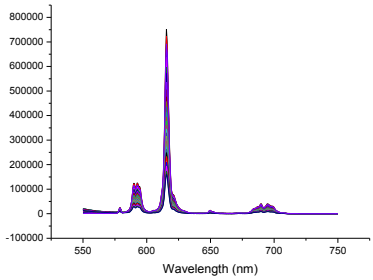

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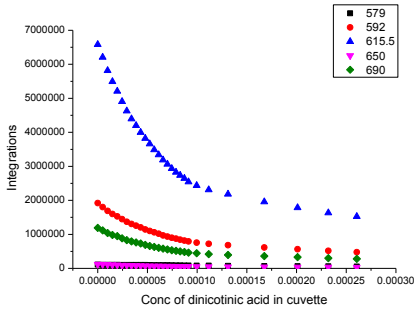
Quenching?	Yes
Stern-Volmer Linear?	No

Binding curve Intensity



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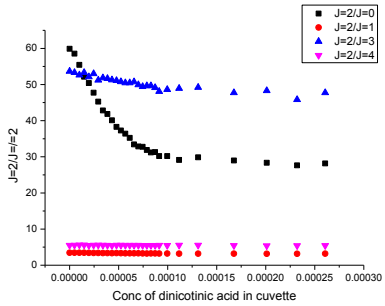
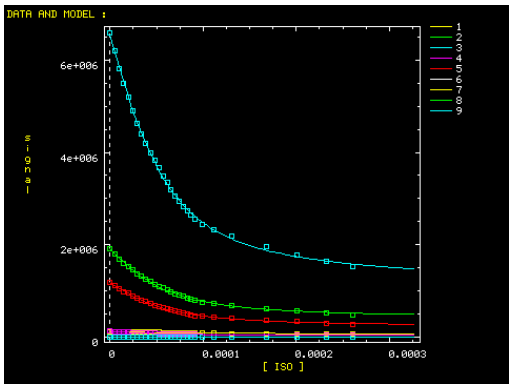
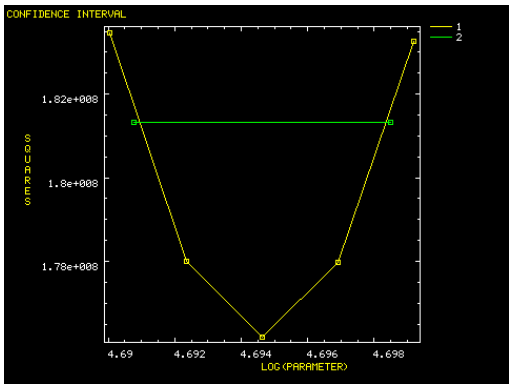


Binding curve Fit

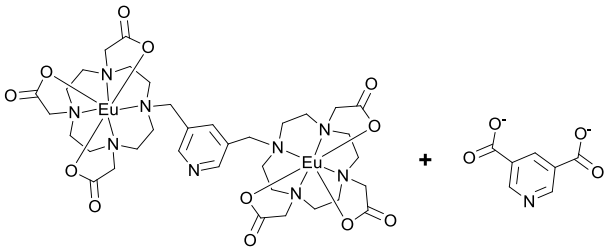


Confidence interval of K



Eu_2.1:6 – PBS pH = 7

Host and Guest



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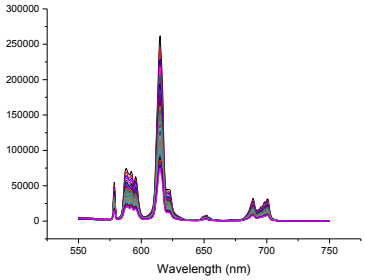
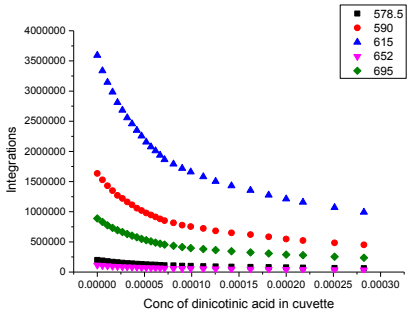
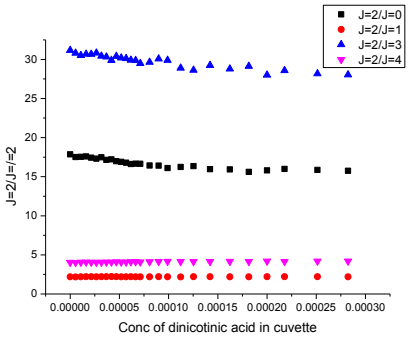


Solvent	PBS buffer pH = 7
Quenching?	Yes
Stern-Volmer Linear?	No

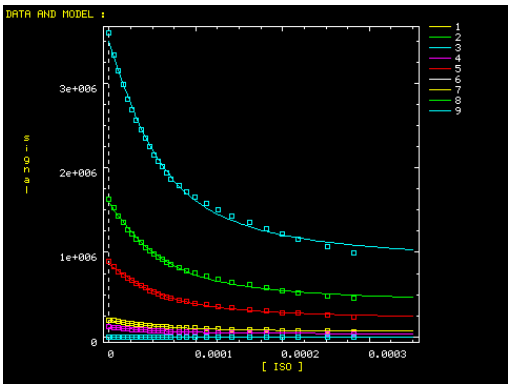
Binding curve Intensity



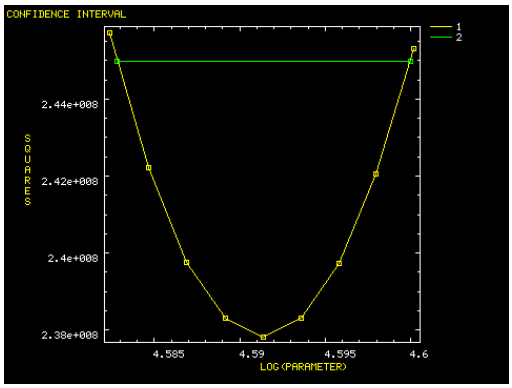
Binding curve I(ΔJ=2)/I(ΔJ=X)



Binding curve Fit

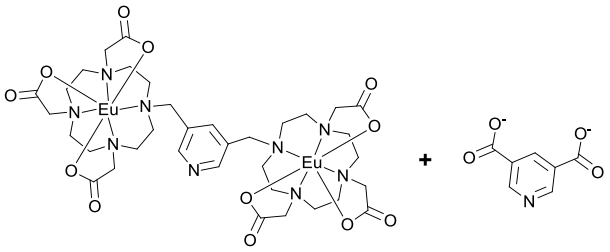


Confidence interval of K



Eu_2.1:6 – PBS pH = 8

Host and Guest



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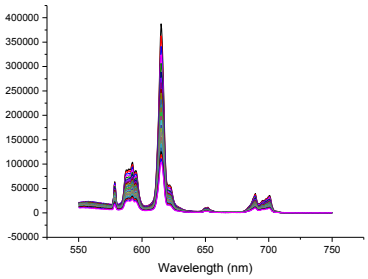
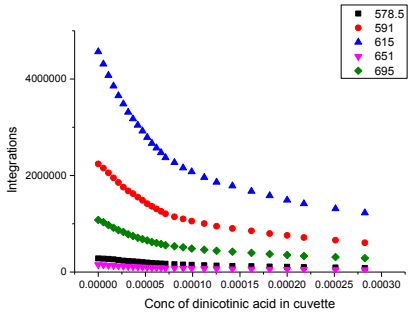
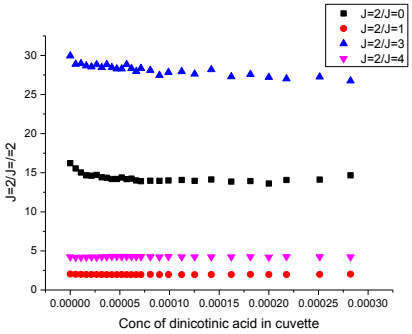


Solvent	PBS buffer pH = 8
Quenching?	Yes
Stern-Volmer Linear?	No

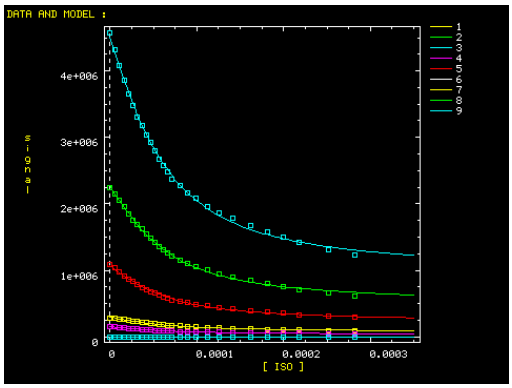
Binding curve Intensity



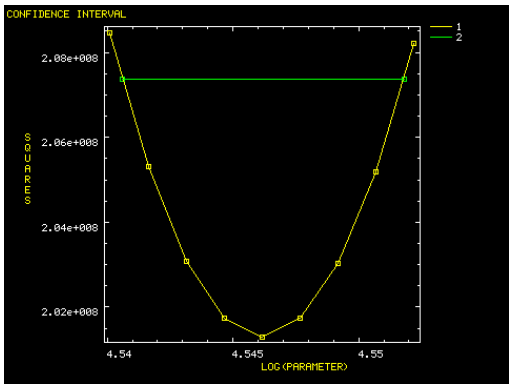
Binding curve I(ΔJ=2)/I(ΔJ=X)



Binding curve Fit

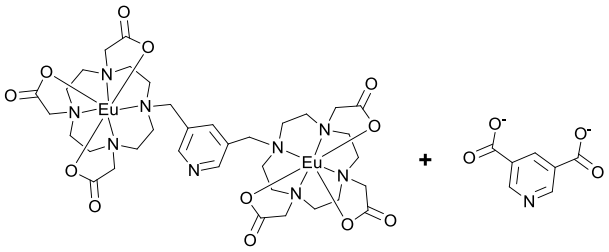


Confidence interval of K

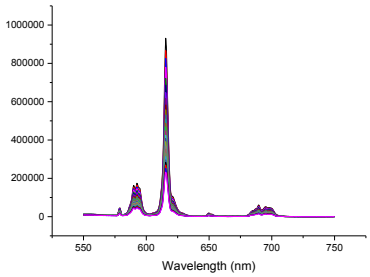


Eu_2.1:6 – PBS pH = 9

Host and Guest

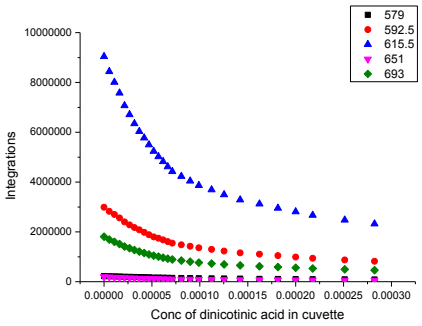


Spectra

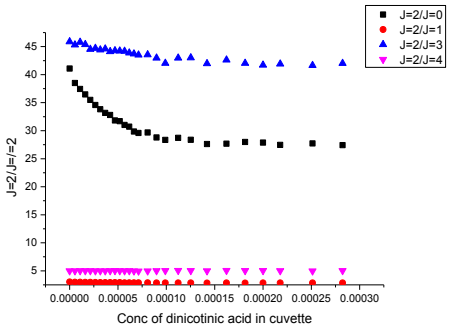


Solvent	PBS buffer pH = 9
Quenching?	Yes
Stern-Volmer Linear?	No

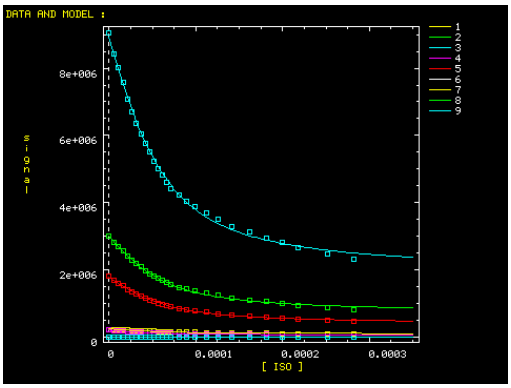
Binding curve Intensity



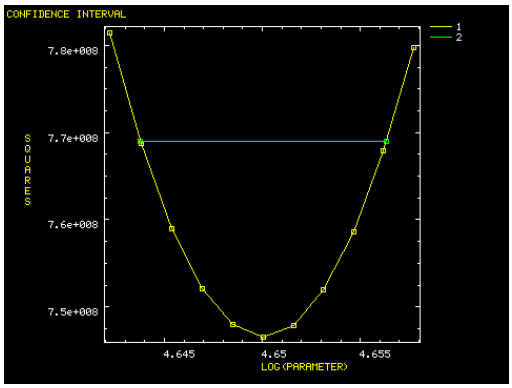
Binding curve I(ΔJ=2)/I(ΔJ=X)



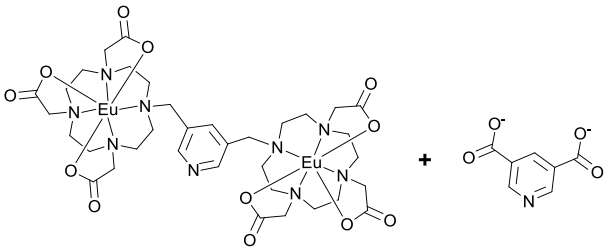
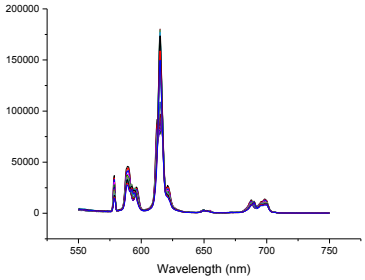
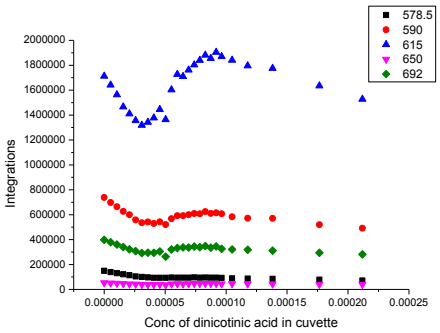
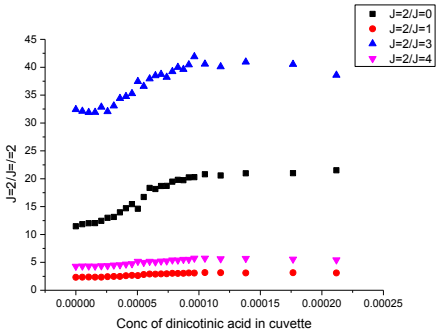
Binding curve Fit



Confidence interval of K

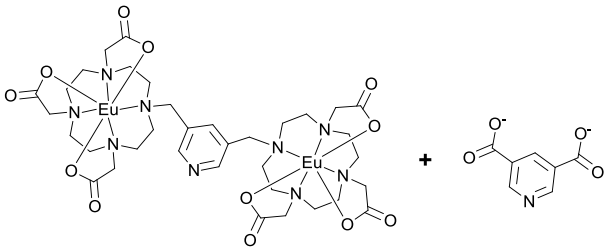


Eu_2.1:6 – HEPES pH = 7

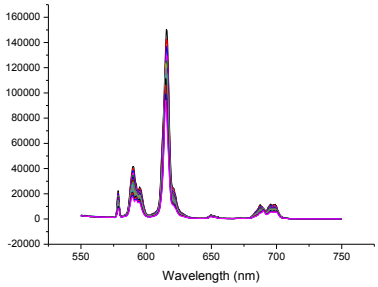
Host and Guest		Spectra	
Solvent	HEPES buffer pH = 7		
Quenching?	Yes		
Stern-Volmer Linear?	No		
Binding curve Intensity		Binding curve I(ΔJ=2)/I(ΔJ=X)	
Binding curve Fit	Could not fit	Confidence interval of K	Could not fit

Eu_2.1:6– HEPES pH = 8

Host and Guest

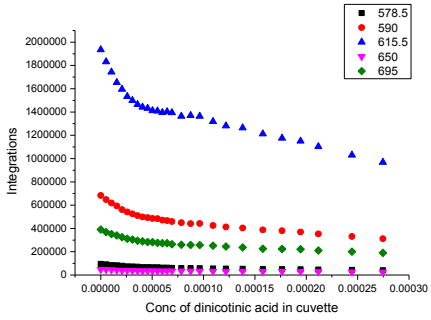


Spectra

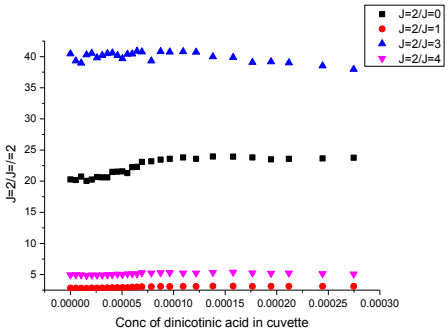


Solvent	HEPES buffer pH = 8
Quenching?	Yes
Stern-Volmer Linear?	Yes, at >3 equivalents

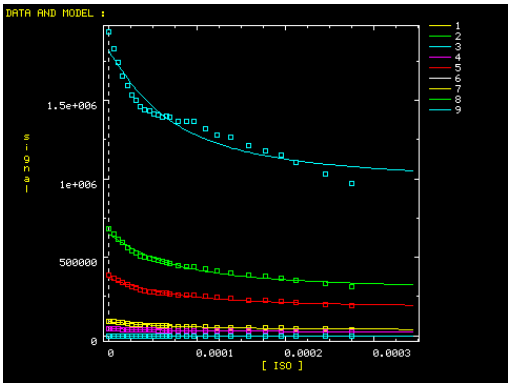
Binding curve Intensity



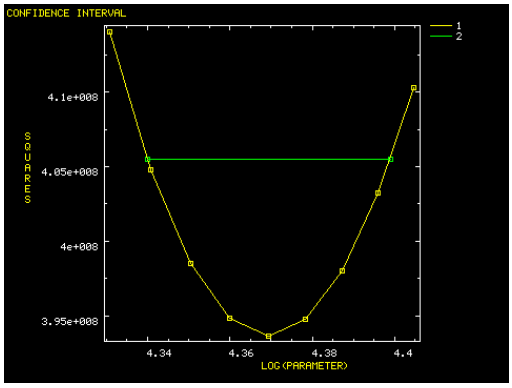
Binding curve I(ΔJ=2)/I(ΔJ=X)



Binding curve Fit

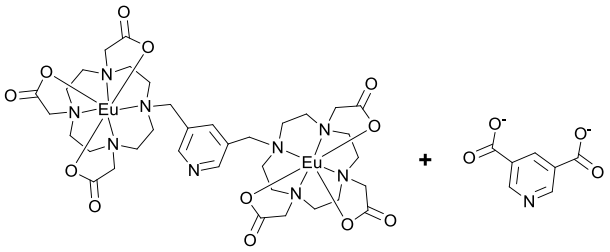


Confidence interval of K

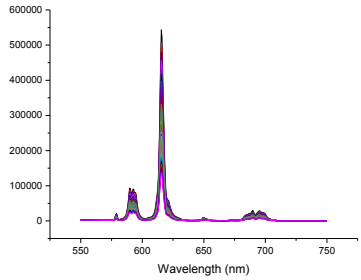


Eu_2.1:6 – HEPES pH = 9

Host and Guest

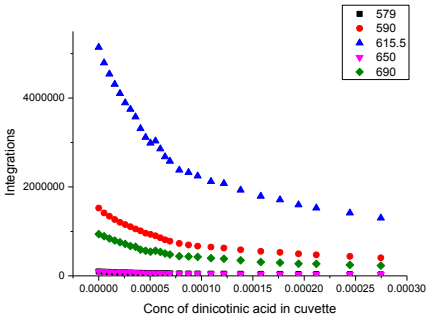


Spectra

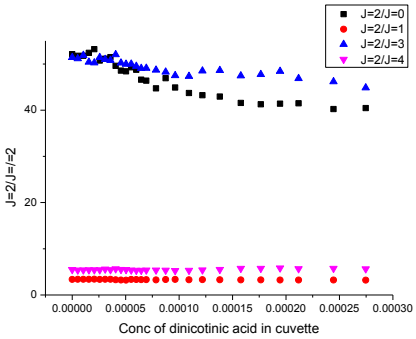


Solvent	HEPES buffer pH = 9
Quenching?	Yes
Stern-Volmer Linear?	Yes, at >3 equivalents

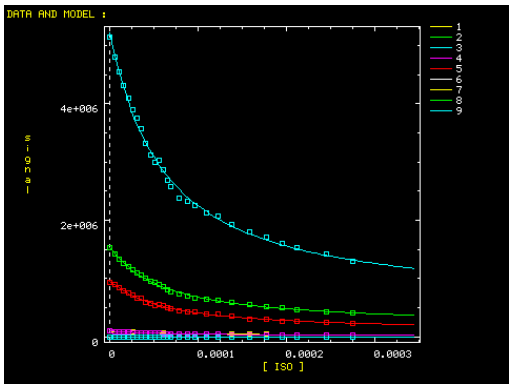
Binding curve Intensity



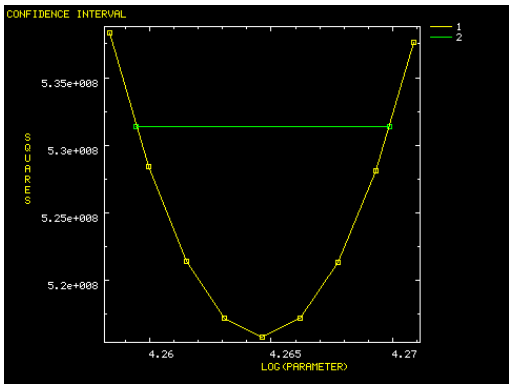
Binding curve I(ΔJ=2)/I(ΔJ=X)



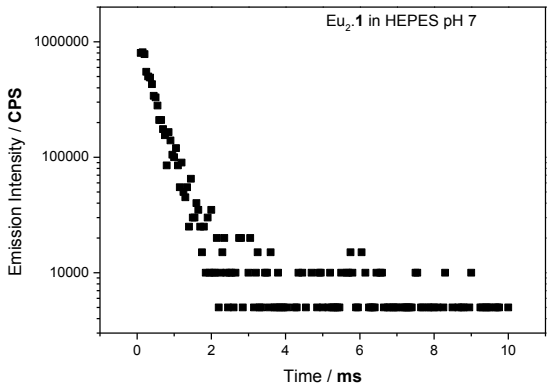
Binding curve Fit

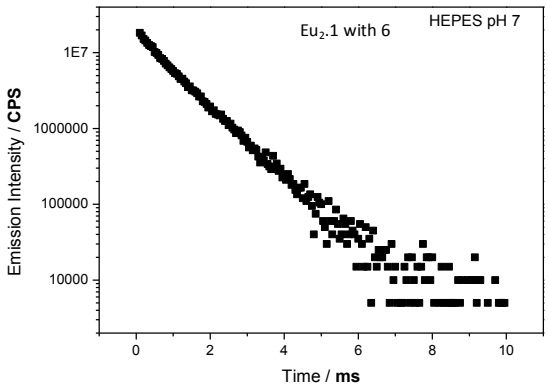


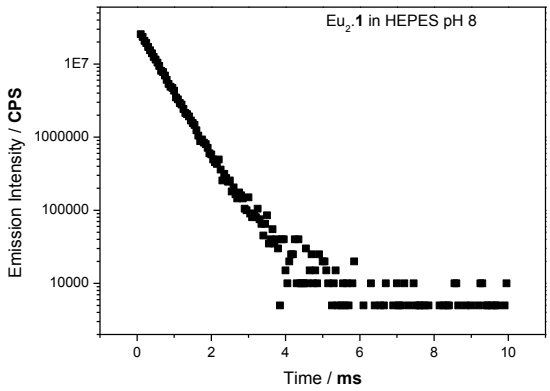
Confidence interval of K

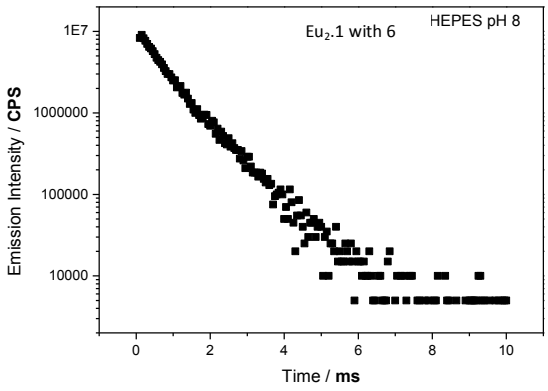


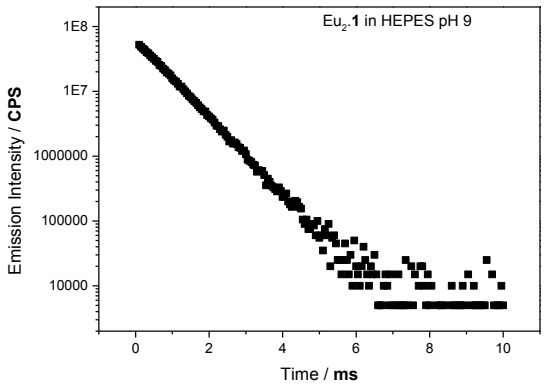
Time-resolved emission intensity profiles

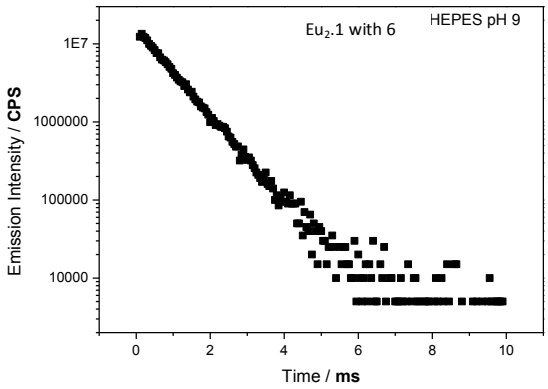


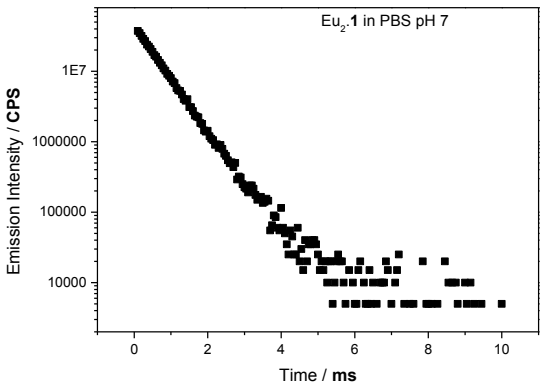


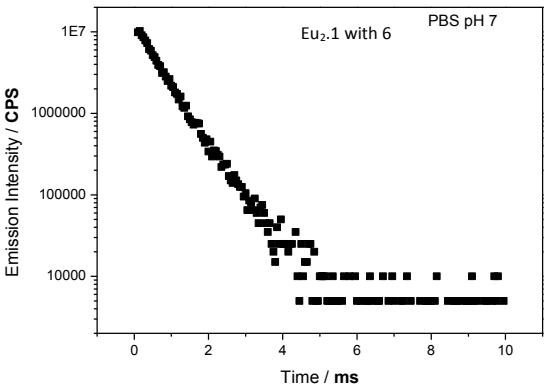









Eu2.1 in PBS pH 7
Emission Intensity / CPS
1E7
1000000
100000
10000
0
2
4
6
8
10
Time / ms


Eu2.1 with 6
PBS pH 7
Emission Intensity / CPS
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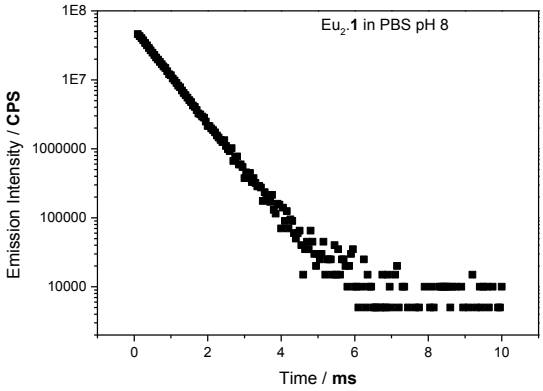
1000000
100000
10000
0
2
4
6
8
10
Time / ms


Eu2.1 in PBS pH 8
Emission Intensity / CPS
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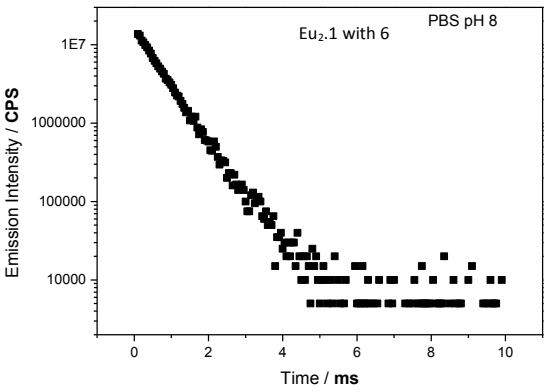
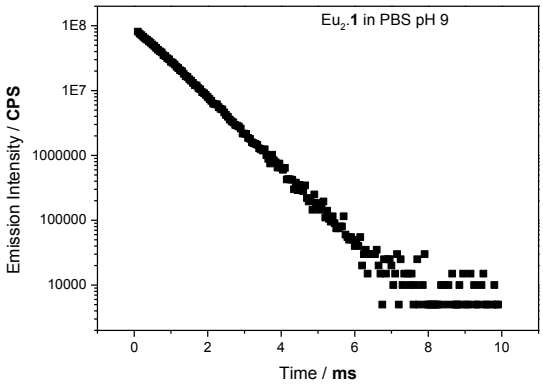
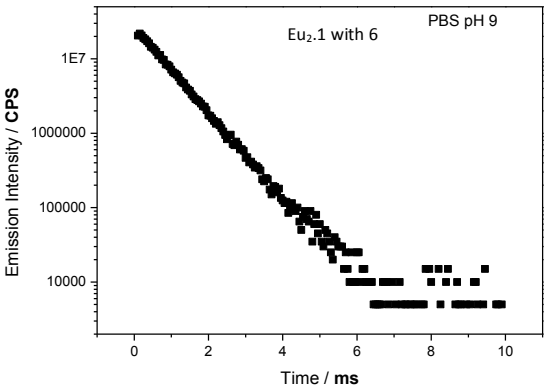
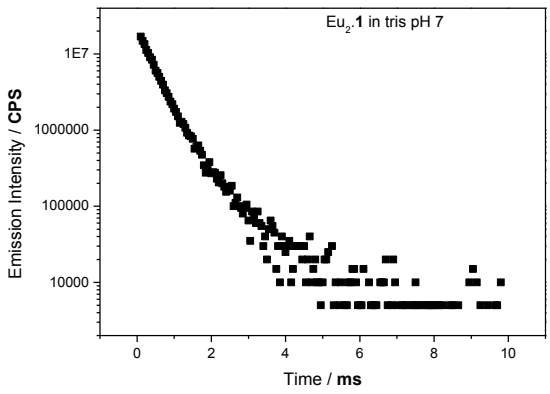
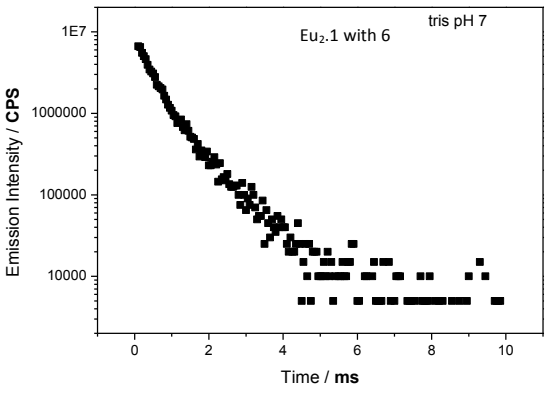
1E7
1000000
100000
10000
0
2
4
6
8
10
Time / ms

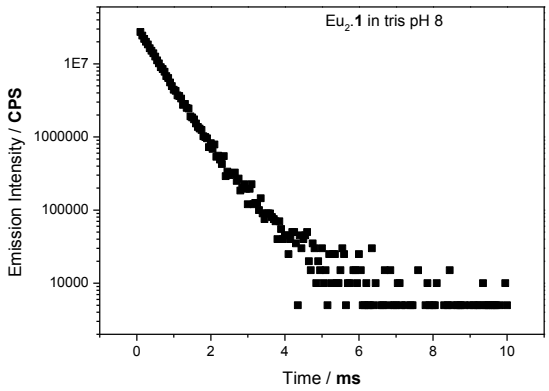

Eu2.1 with 6
PBS pH 8
Emission Intensity / CPS
1E7
1000000
100000
10000
0
2
4
6
8
10
Time / ms

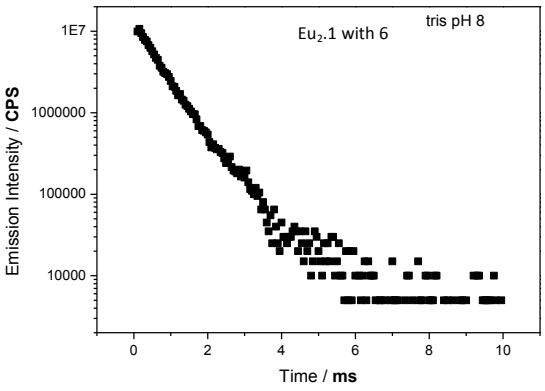

Eu2.1 in PBS pH 9
Emission Intensity / CPS
1E8
1E7
1000000
100000
10000
0
2
4
6
8
10
Time / ms

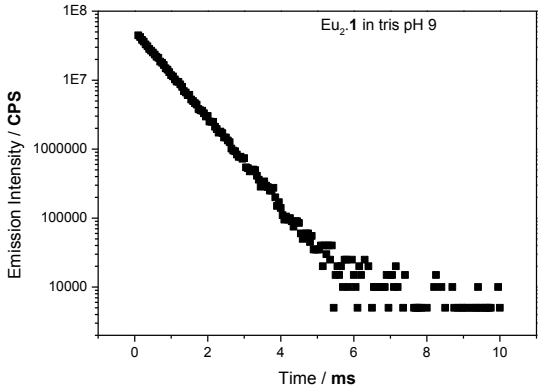

Eu2.1 with 6
PBS pH 9
Emission Intensity / CPS
1E7
1000000
100000
10000
0
2
4
6
8
10
Time / ms

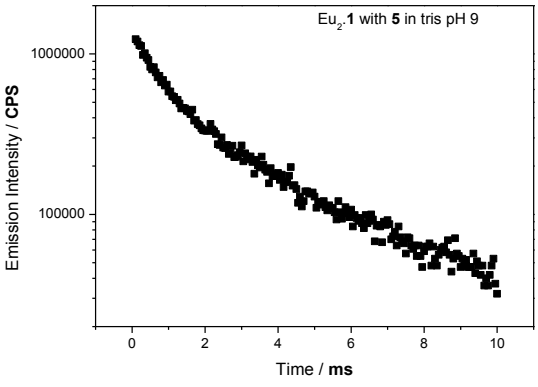

Eu2.1 in tris pH 7
Emission Intensity / CPS
1E7
1000000
100000
10000
0
2
4
6
8
10
Time / ms

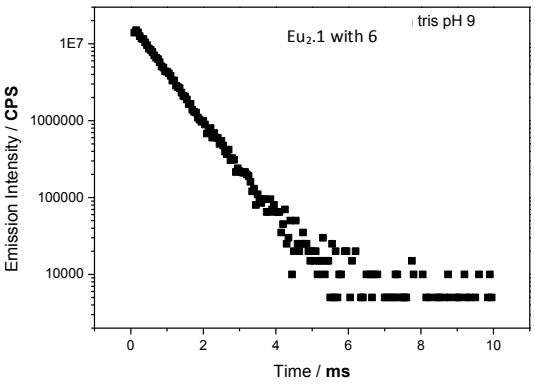

tris pH 7
Eu2.1 with 6
Emission Intensity / CPS
1E7
1000000
100000
10000
0
2
4
6
8
10
Time / ms

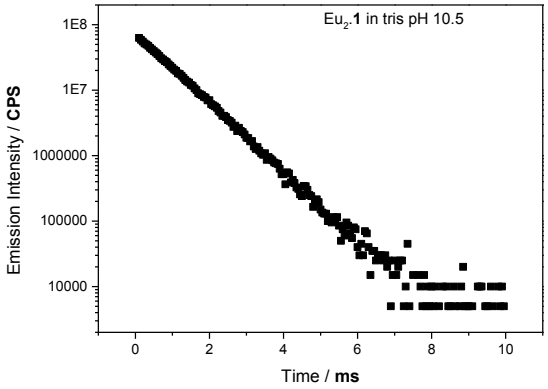

Eu2.1 in tris pH 8
Emission Intensity / CPS
1E7
1000000
100000
10000
0
2
4
6
8
10
Time / ms

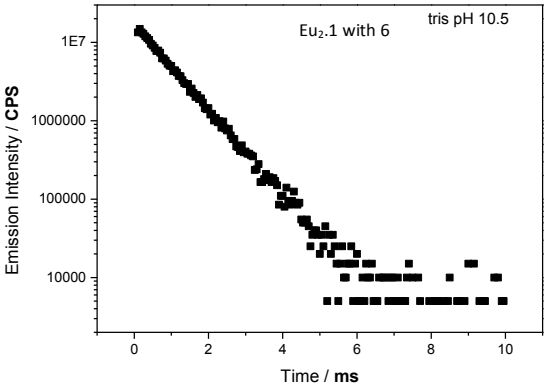

tris pH 8
Eu2.1 with 6
Emission Intensity / CPS
1E7
1000000
100000
10000
0
2
4
6
8
10
Time / ms

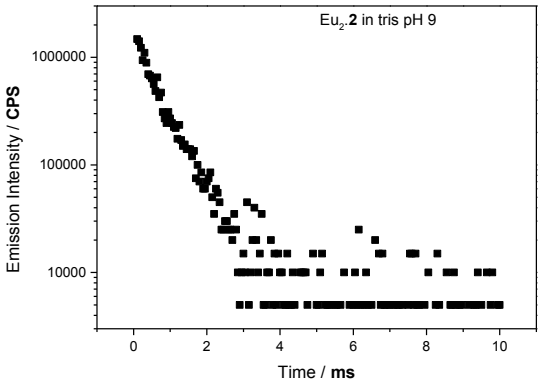

Eu2.1 in tris pH 9
Emission Intensity / CPS
1E8
1E7
1000000
100000
10000
0
2
4
6
8
10
Time / ms

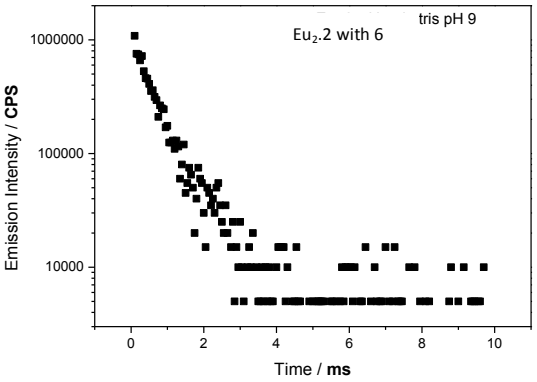

Eu2.1 with 5 in tris pH 9
Emission Intensity / CPS
1000000
100000
0
2
4
6
8
10
Time / ms

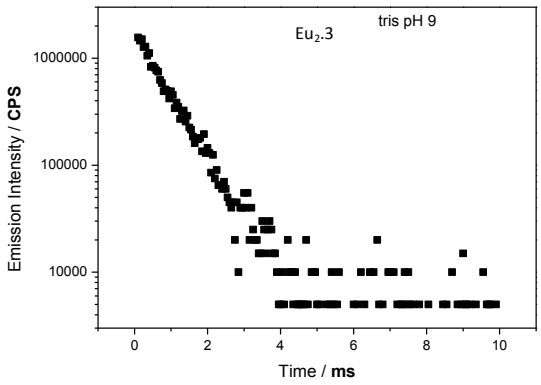

tris pH 9
Eu2.1 with 6
Emission Intensity / CPS
1E7
1000000
100000
10000
0
2
4
6
8
10
Time / ms

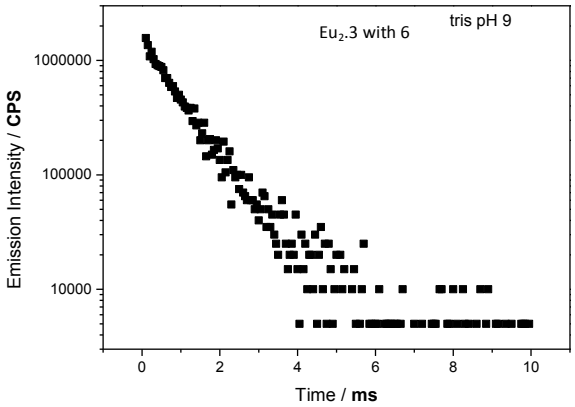

Eu2.1 in tris pH 10.5
Emission Intensity / CPS
1E8
1E7
1000000
100000
10000
0
2
4
6
8
10
Time / ms

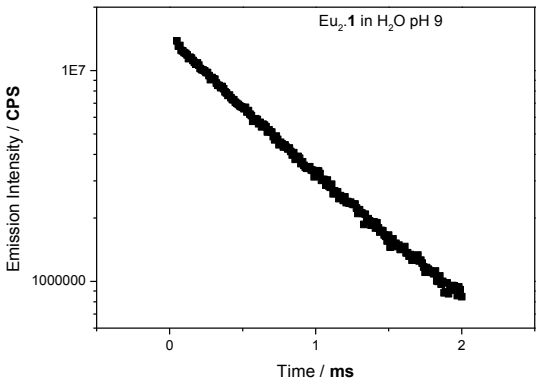

tris pH 10.5
Eu2.1 with 6
Emission Intensity / CPS
1E7
1000000
100000
10000
0
2
4
6
8
10
Time / ms

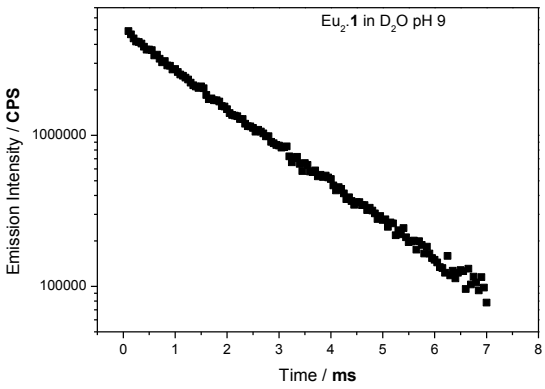

Eu2.2 in tris pH 9
Emission Intensity / CPS
1000000
100000
10000
0
2
4
6
8
10
Time / ms

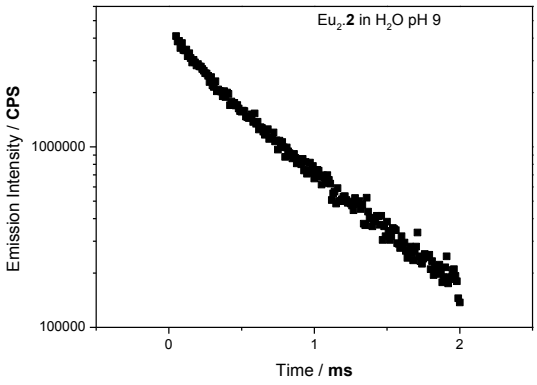

tris pH 9
Eu2.2 with 6
Emission Intensity / CPS
1000000
100000
10000
0
2
4
6
8
10
Time / ms

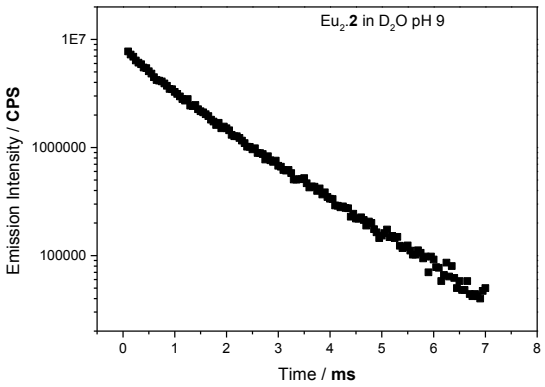

tris pH 9
Eu2.3
Emission Intensity / CPS
1000000
100000
10000
0
2
4
6
8
10
Time / ms

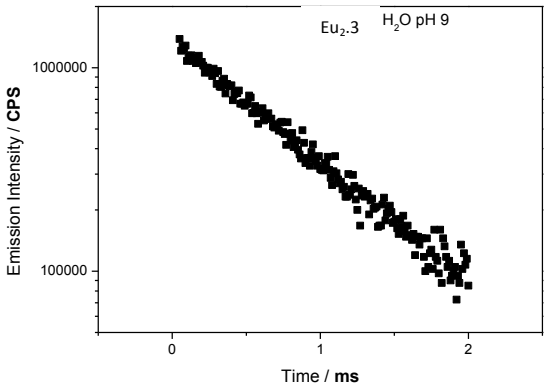

tris pH 9
Eu2.3 with 6
Emission Intensity / CPS
1000000
100000
10000
0
2
4
6
8
10
Time / ms

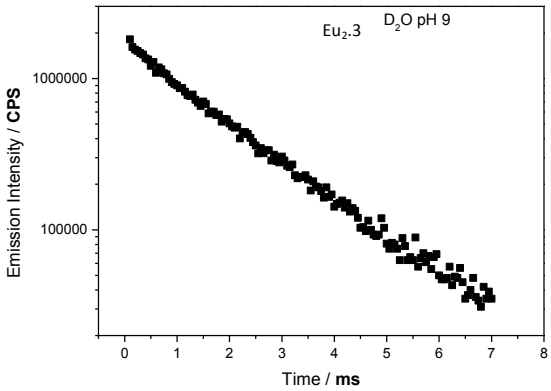

Eu2.1 in H2O pH 9
Emission Intensity / CPS
1E7
1000000
0
1
2
Time / ms


Eu2.1 in D2O pH 9
Emission Intensity / CPS
1000000
100000
0
1
2
3
4
5
6
7
8
Time / ms


Eu2.2 in H2O pH 9
Emission Intensity / CPS
1000000
100000
0
1
2
Time / ms


Eu2.2 in D2O pH 9
Emission Intensity / CPS
1E7
1000000
100000
0
1
2
3
4
5
6
7
8
Time / ms


Eu2.3 H2O pH 9
Emission Intensity / CPS
1000000
100000
0
1
2
Time / ms


Eu2.3 D2O pH 9
Emission Intensity / CPS
1000000
100000
0
1
2
3
4
5
6
7
8
Time / ms

Dynafit script example

```
[task]
task = fit
data = equilibria

[mechanism]
Eu + ISO <==> complex1 : K1 assoc

[constants]
K1 = 3e5 ??

[concentrations]
Eu = 2.2E-05 ?

[responses]
Eu = 26000 , complex1 = 0

[equilibria]
variable ISO
file C:\Users\TJS\Desktop\Leila\partII\iso263\f1.txt | response Eu = 0.302e10 ?  , complex1 = 10e8 ?
file C:\Users\TJS\Desktop\Leila\partII\iso263\f2.txt | response Eu = 0.302e10 ?  , complex1 = 10e8 ?
file C:\Users\TJS\Desktop\Leila\partII\iso263\f3.txt | response Eu = 0.302e10 ?  , complex1 = 10e8 ?
file C:\Users\TJS\Desktop\Leila\partII\iso263\f4.txt | response Eu = 0.302e10 ?  , complex1 = 10e8 ?
file C:\Users\TJS\Desktop\Leila\partII\iso263\f5.txt | response Eu = 0.302e10 ?  , complex1 = 10e8 ?
;file C:\Users\TJS\Desktop\Leila\partII\iso263\f6.txt | response Eu = 0.302e10 ?  , complex1 = 10e8 ?
;file C:\Users\TJS\Desktop\Leila\partII\iso263\f7.txt | response Eu = 0.302e10 ?  , complex1 = 10e8 ?
;file C:\Users\TJS\Desktop\Leila\partII\iso263\f8.txt | response Eu = 0.302e10 ?  , complex1 = 10e8 ?
;file C:\Users\TJS\Desktop\Leila\partII\iso263\f9.txt | response Eu = 0.302e10 ?  , complex1 = 10e8 ?

[output]

directory C:\Users\TJS\Desktop\Leila\partII\iso263\results
```