Interaction of Cd(II) and Ni(II) terpyridine complexes with model polynucleotides:

a multidisciplinary approach

Giampaolo Barone • Giuseppe Gennaro • Anna Maria Giuliani • Mauro Giustini

G. Barone • G. Gennaro • A.M. Giuliani

Dipartimento STEBICEF, Università di Palermo, 90128 Palermo, Italia

M. Giustini (✉)

Dipartimento di Chimica, Università "La Sapienza", P.le A. Moro 5, 00185 Roma, Italia

Tel: +39 06 49913336

Fax: +39 06 490324

email: mauro.giustini@uniroma1.it

Electronic Supplementary Information

S.1. Synthesis and characterization of cadmium and nickel complexes

Cd(terpy)Cl_2 (complex **1**) was prepared according to literature procedures[1,2] by reacting 0.98mmol of $CdCl_2$ with equimolar terpyridine in water at 363K. A light yellow precipitate was obtained, separated, washed and dried: the yield was 80.9%. The product was very scarcely soluble in water, as expected for a neutral complex.

Elemental analysis. Calculated for $C_{15}H_{11}N_3Cl_2Cd$ (**1**): C= 43.24%; H= 2.66%; N= 10.09%; experimental: C= 43.65%; H= 2.64%; N= 10.03%.

The nickel-terpyridine complex Ni(terpy)$Cl_2 \cdot 3H_2O$ (complex **2**) was prepared following literature procedures;[3,4] a slight excess of $NiCl_2 \cdot 6H_2O$ was used to avoid formation of bis(terpyridine)complexes.[3] Complex **2** was synthesized in ethanol solution at 343K: a blue-green crystalline product was obtained with 65% yield. The complex is very soluble in water.

Elemental analysis. Calculated for $C_{15}H_{17}N_3O_3Cl_2Ni$ (**2**)**:** C= 43.21%; H= 4.11%; N= 10.08%; experimental: C= 43.10%; H= 4.34%; N= 10.06%.

S.2. FT-IR spectra

The IR spectra (KBr pellets) of terpy, complex **1** and complex **2**, together with a Table of the most significant vibrations with the assignments, are presented in Fig S1 and Table S1. The assignments are based on literature data.[5]

The presence of shifted terpyridine bands in the IR spectra of **1** and **2** is a clear evidence of the metal complexation. The spectra of **2** exhibit also a broad intense OH stretching band centred at $3250 cm^{-1}$ (not shown), due to the three water molecules present in the complex. The most interesting metal-chlorine stretching bands are very neatly observed for the cadmium complex at 269 and $253 cm^{-1}$, in agreement with the literature data.[6] Two medium intensity bands at 256 and $246 cm^{-1}$ can tentatively be assigned to Ni-Cl stretching vibrations for complex **2**.[7] With the aid of the IR data pertinent to Ir-N stretchings in the $[Ir(terpy)_2](ClO_4)_3 \cdot H_2O$ complex,[5] Ni-N stretchings were identified in the spectra of **2**. Indeed, on the basis of literature data for related complexes[7] the stretching frequencies for the Ni-N and Ir-N bonds should not be substantially different; moreover similar Ni-N stretching frequencies have been reported for other octahedral Ni(II) complexes.[8] The assignments for complex **1** were made accordingly, by analogy. In the case of $Cd(terpy)Cl_2$ only one band at $309 cm^{-1}$ was observed in the relevant IR spectral region, at a frequency nicely in between the values reported for octahedral and tetrahedral ammine complexes of Cd(II)[9] while the other bands reported in the literature[6] were outside the available range.

Table S1.
Some representative vibrations [a] of terpyridine ligand shifted upon complex formation

Terpy	Complex **1**	Complex **2**	Assignments
1581 vs	1590 vs	1598 vs	CC ring stretch
1265 m	1249 s, b	1253 m	CCN ring stretch
989 m	1014 s	974 w 1017 m, s	CC ring stretch
632 m	658 m	669 w	CCN in plane def.
622 m	650 m,s	649 m, w	
615 w	638 m,s	642 m	
510 m	511 m, w	511 w	
399 m, s	399 m, w	442 w	
	309 w	373 w,b, 324 w 304 w	Me-N stretch
	269 m, 253m	(256* m, 246* m)	Me-Cl stretch

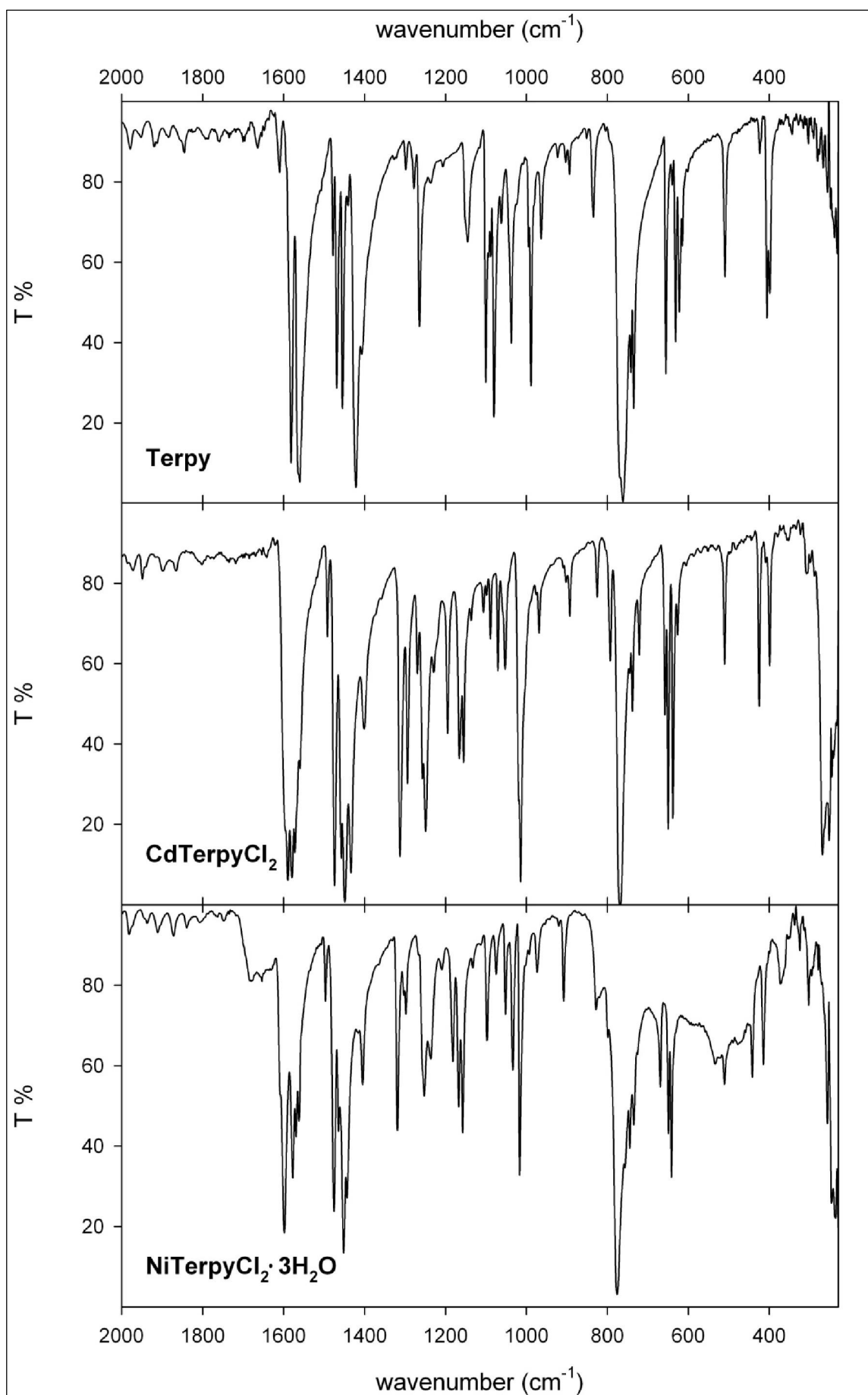[a] wavenumbers in cm^{-1} - * tentative assignments

Fig. S1 FT-IR spectra (KBr pellet) of the ligand and its metal complexes.

S.3. Thermogravimetric analysis

The thermograms of the complexes **1** and **2** were obtained under N_2 flux in the temperature range 300-1170K, with an heating rate of either 5K/min (complex **1**) or 10K/min (for **2**); the relevant data are collected in Table S2. Complex **2** lost water in two steps, the first corresponding to hydration water (324 K, $1H_2O$) and the second to coordinated water (369K, $2H_2O$), confirming the analytical results and in agreement with the X-ray obtained formula:[4] thus the nickel complex prepared can be formulated as $[Ni(terpy)(H_2O)_2Cl]Cl \cdot H_2O$, as expected.

The thermogravimetric analysis yielded also an unexpected and previously not reported decomposition scheme for both **1** and **2**, involving as a first step the loss of metal chloride (either $CdCl_2$ at 688K for **1**, or ½ $NiCl_2$ at 729K for **2**). This step was followed by the progressive loss of terpy leaving no residue in the case of complex **1**. In the case of complex **2**, the first loss seemingly yielded the corresponding bis-terpyridine complex, that would loose the terpyridine ligand in the following step, leaving a residue of ½ $NiCl_2$.

The percent weight losses for the nickel complex did not match exactly the calculated values, even though they were not dramatically different. The first stage of the thermal decomposition might possibly not involve the whole *mono*-terpyridine complex; this would also explain the percent weight of the residue, higher than expected for half $NiCl_2$. The different behaviour of the two complexes after the first thermal loss is in agreement with the almost complete absence of any literature report of simple bis-terpyridine complexes of Cd(II).

Table S2
Terpyridine and its complexes with cadmium and nickel: thermogravimetric results

Compound	T, K	Weight loss, % [a]	Mass loss, Da [a]
1 M.W. 416.6Da	688	44.8 (44.0)	186.8 (183.3)
	868	45.8 ⌉	190.8 ⌉
	>920	├ (56.0)	├ (233.3)
		8.9 ⌟	37.1 ⌟
2 M.W. 416.9Da	369	8.7 (8.6)	36.2 (36.0)
	729	14.5 (15.5)	60.4 (64.8)
	906	57.7 (56.0)	240.5 (233.3)
	residue at 1170K	19.1 (15.5)	79.6 (64.8)
Terpy M.W. 233.3Da	480 [b]	98.7	230.3 (233.3)

[a] in parentheses the losses calculated for the decomposition scheme outlined in the text.
[b] Literature value for 5% loss: 498K.[10]

S.4. Electronic spectra

The UV-Vis spectra of terpy (in ethanol, because of its poor solubility in water) and of complexes **1** and **2** (in aqueous solution) have been collected at room temperature in the region 200-350nm. In Table S3 the relevant spectral data are reported. The molar absorbance values for complex **2** compare reasonably well with the literature data reported for the bis[α-terpyridine-ω-methylpoly(ethylene glycol)] Ni(II) hexafluorophosphate in water.[11]
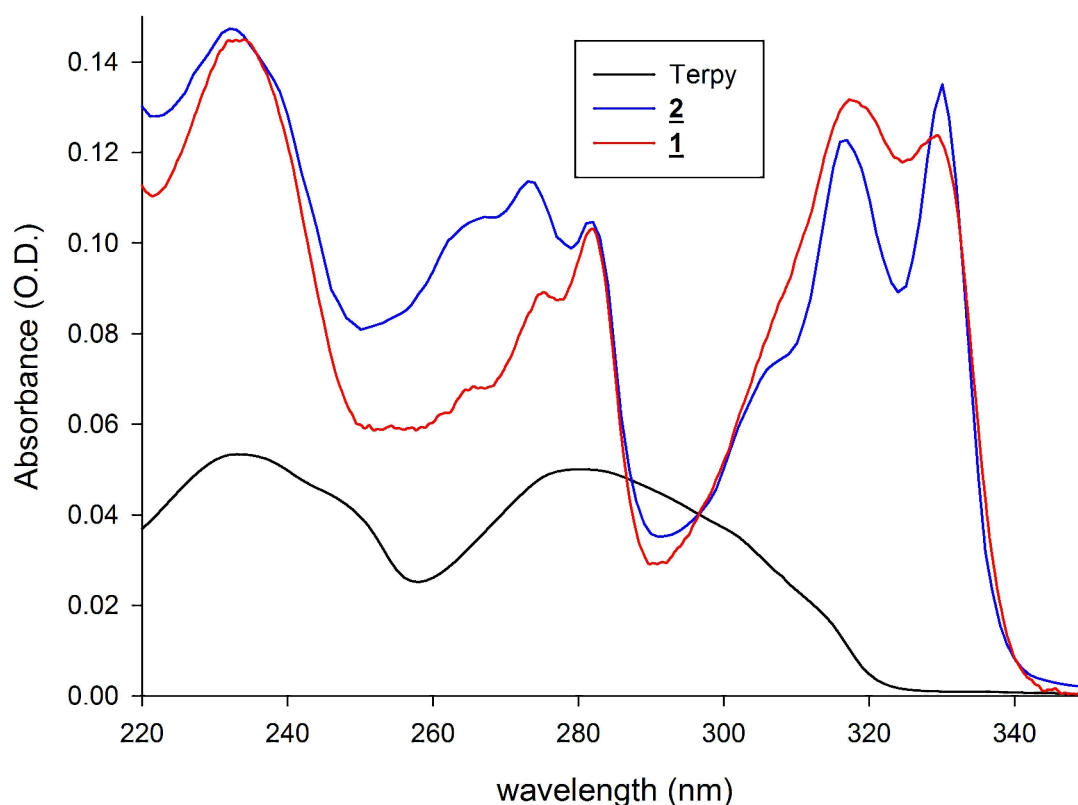

Fig. S2 UV absorption spectra of terpyridine (2.5 µM), complex **1** (7.1 µM) and complex **2** (6.9 µM).

Table S3
UV-Vis data of terpyridine and its complexes with cadmium and nickel
(λ in nm; in parentheses the calculated ε values in $M^{-1}cm^{-1}$).

Terpy λ	Complex **1** λ (ε)	Complex **2** λ (ε)
233 $(2.23 \cdot 10^4)^\S$	232 $(2.13 \cdot 10^4)$	233 $(2.08 \cdot 10^4)$
		274 $(1.65 \cdot 10^4)$
280 $(2.09 \cdot 10^4)^\S$	282 $(1.40 \cdot 10^4)$	282 $(1.52 \cdot 10^4)$
	319 $(1.81 \cdot 10^4)$	319 $(1.83 \cdot 10^4)$
	330 $(1.72 \cdot 10^4)$	330 $(1.98 \cdot 10^4)$

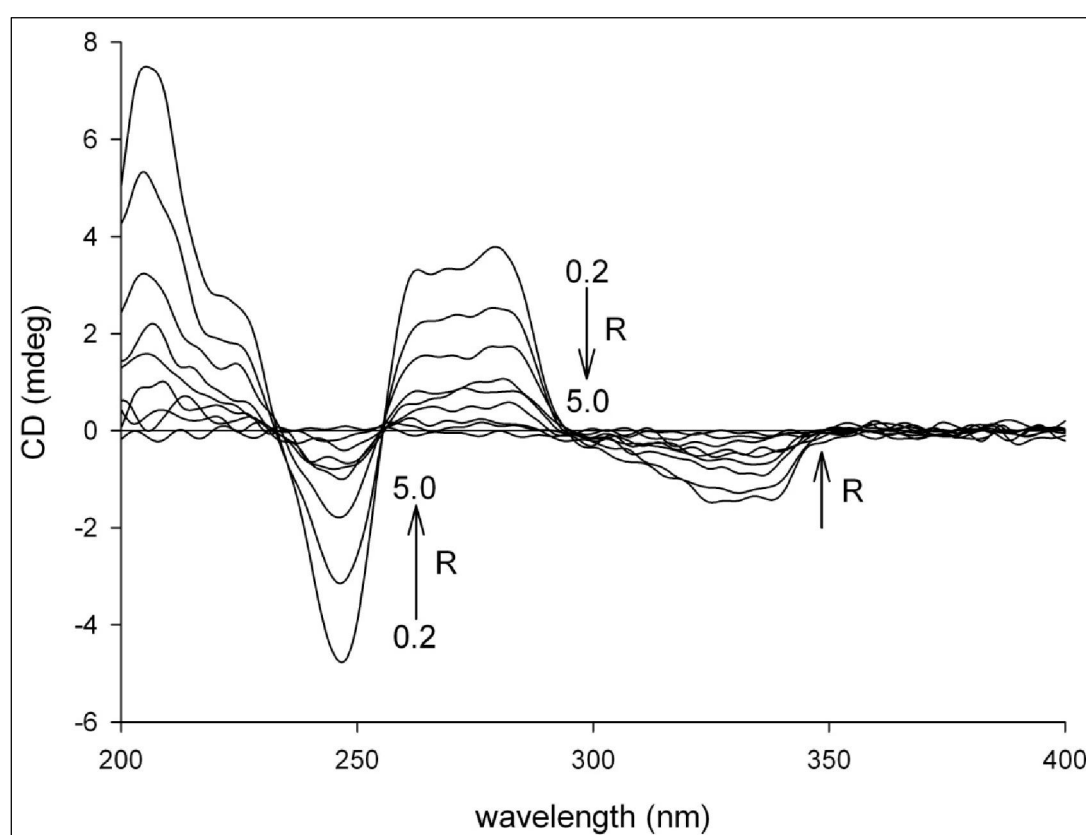§ ε values from ref. 12.

S.5. Supplementary data of Circular dichroism and absorption spectroscopy

Fig. S3 CD spectra of Cd(terpy)Cl$_2$ titrated with polyAT. [Cd(terpy)Cl$_2$]= 6.25 µM; Tris 1.0 mM at pH 7.8 - NaCl 2 mM; l= 1.0 cm; T= 298 K.
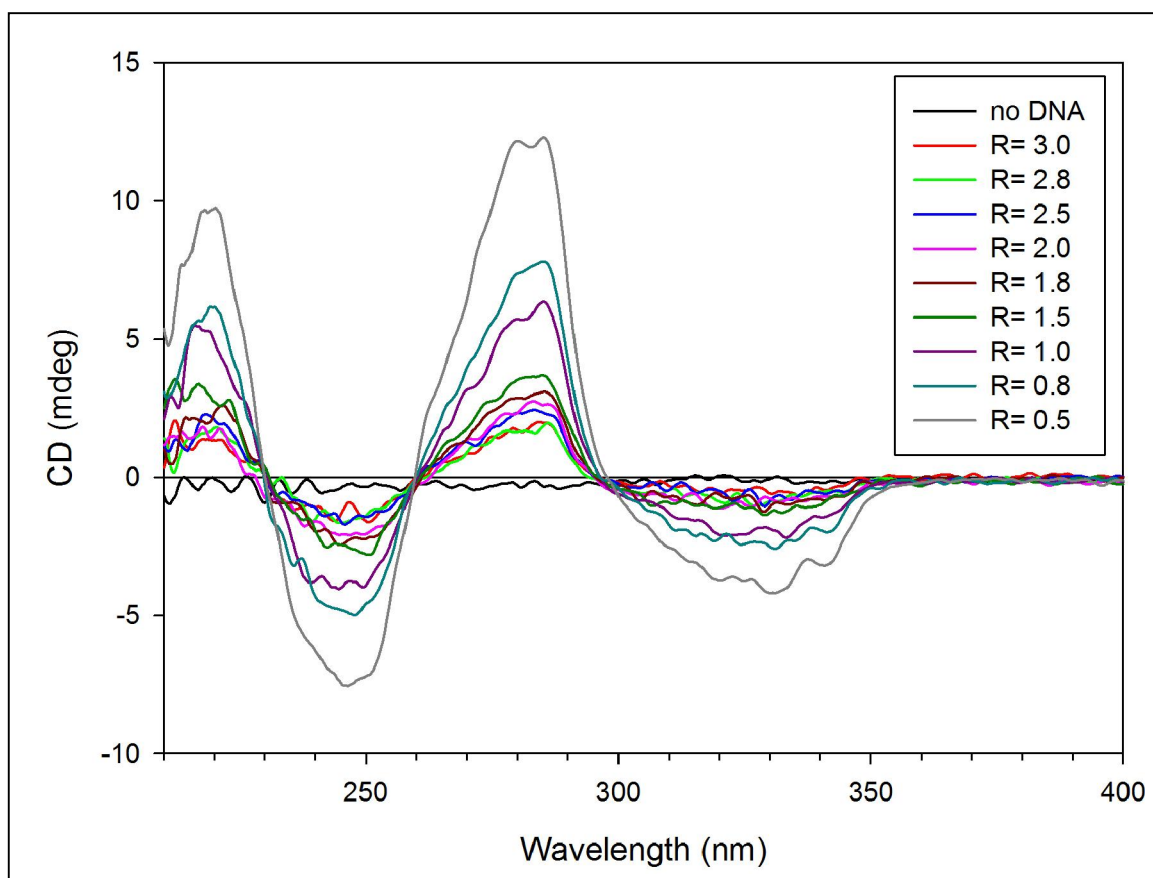
Fig. S4 Titration of Cd(terpy)Cl$_2$ with ct-DNA. Lyophilized ct-DNA (dialyzed as described in the literature[13]) concentration has been obtained by UV spectroscopy (ε_{260}= 6600 M^{-1}cm^{-1}).[14] R= [Cd(terpy)Cl$_2$]/[ct-DNA]$_P$; [Cd(terpy)Cl$_2$]= 6.25·10^{-5} M - Tris 1.0 mM at pH 7.5 - NaCl 2 mM; l= 1.0cm; T= 298 K.
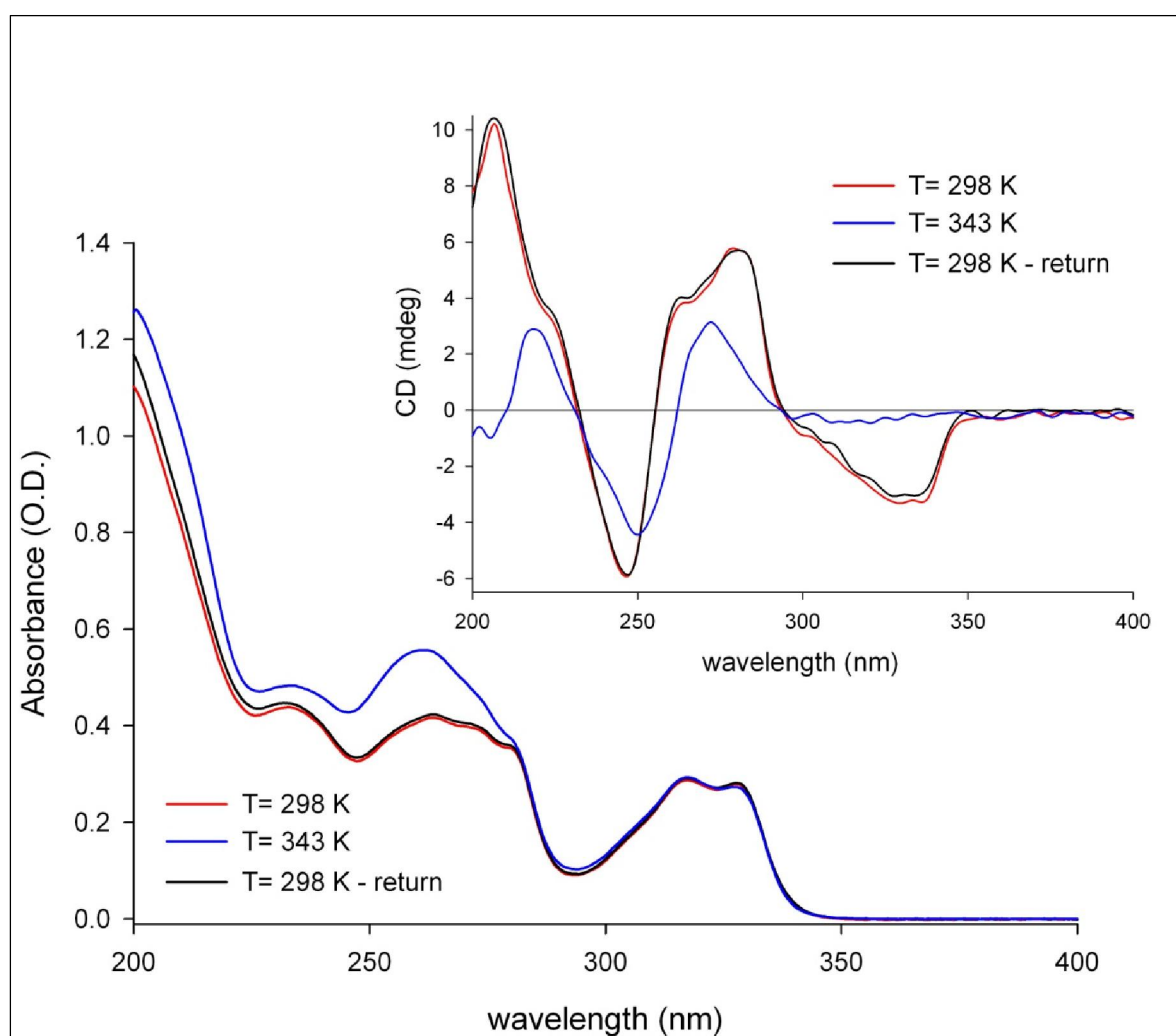
Fig. S5 UV-Vis and CD (inset) spectra of the system Cd(terpy)Cl$_2$/polyAT (R= 0.5).

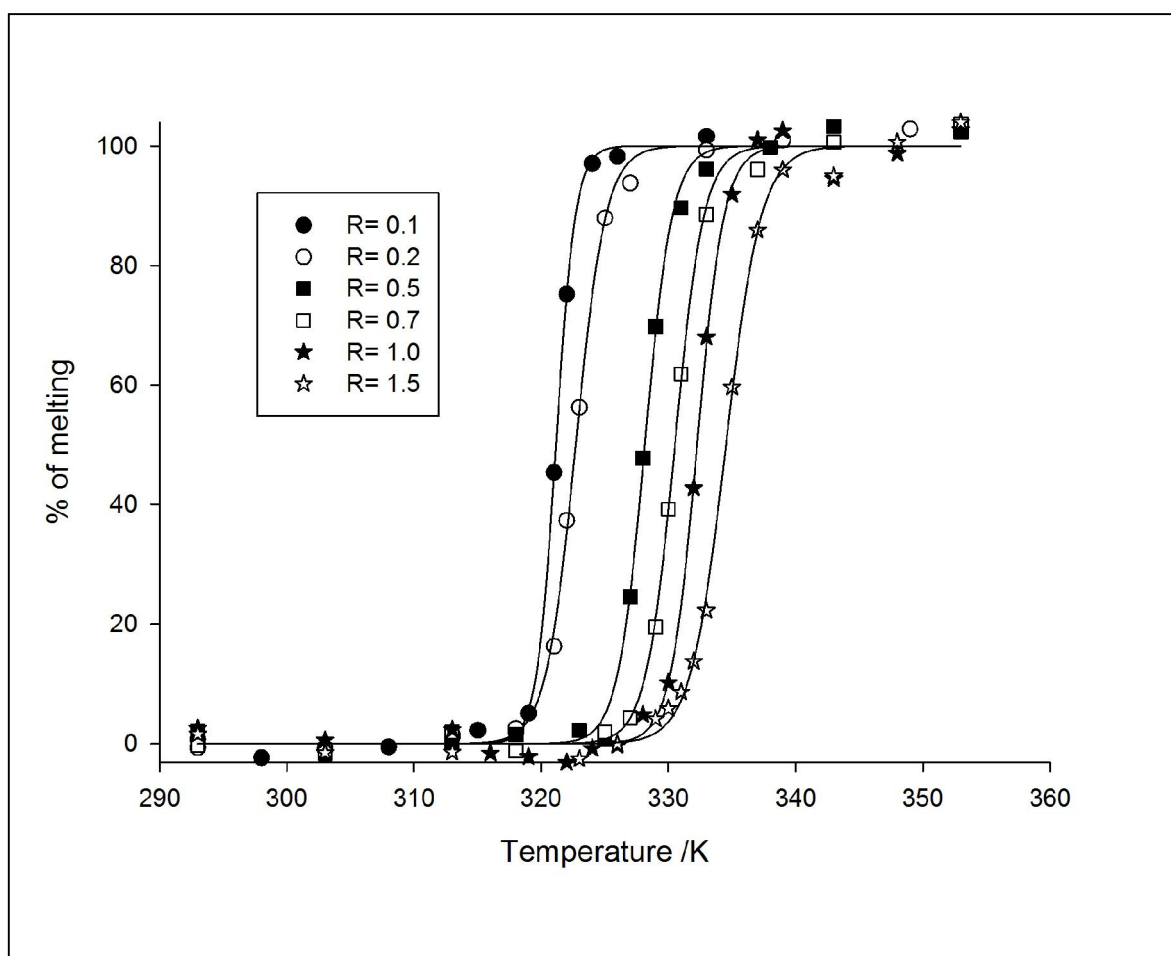[polyAT]$_P$= 41.3 µM; Tris 1.0 mM at pH 7.3 - NaCl 2 mM; l= 1.0 cm.

S.6. PolyAT melting in the presence of <u>1</u>.

Fig. S6 Normalized melting profiles for the polyAT-Cd(terpy)Cl$_2$ system in 1 mM Tris-10 mM NaCl (pH= 7.5±0.3).

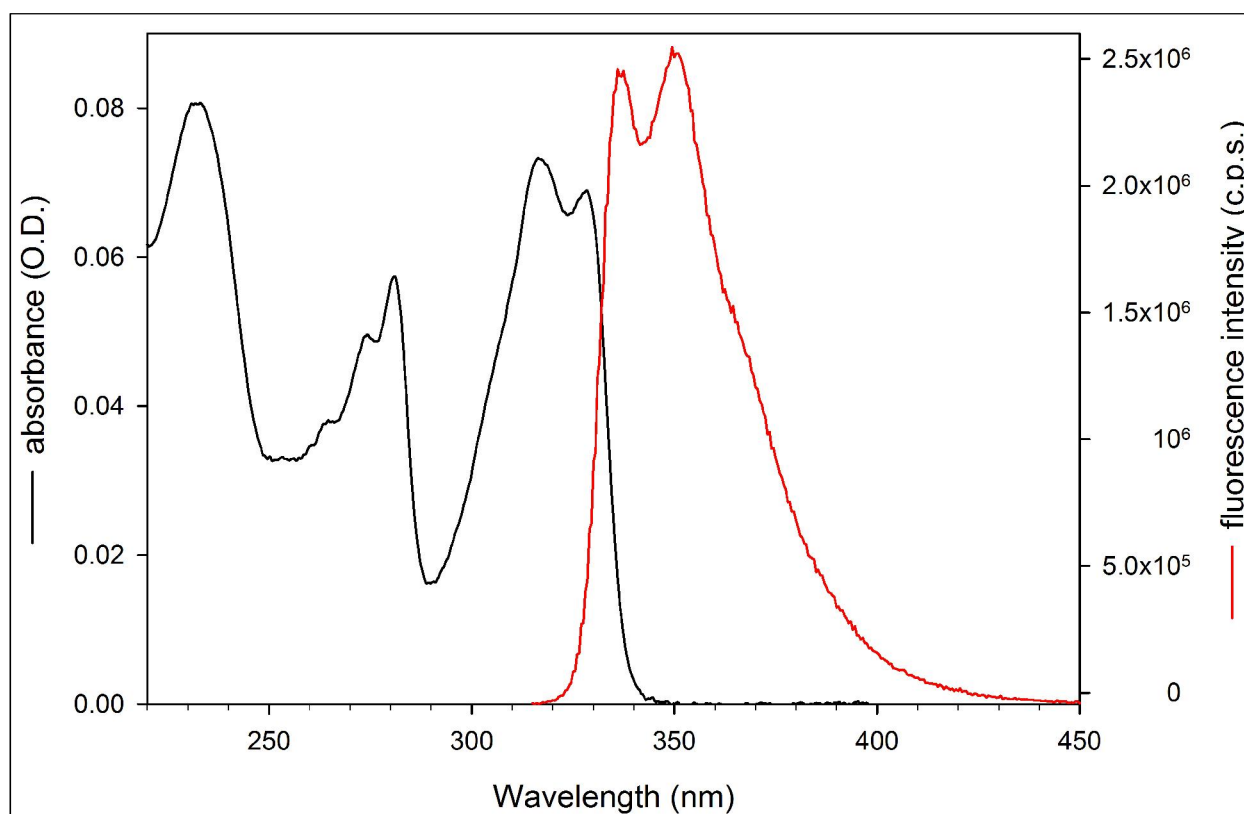### S.7. Supplementary data of fluorescence spectroscopy

Fig. S7 UV-vis (left hand axis) and emission (right hand axis) spectra of a 3.8 µM solution of Cd(terpy)Cl$_2$ in Tris 1.0 mM at pH 7.5 - NaCl 2 mM; l= 1.0 cm; T= 298 K; λ_{ecc}= 280 nm; slits: 1.5/1.5 nm.
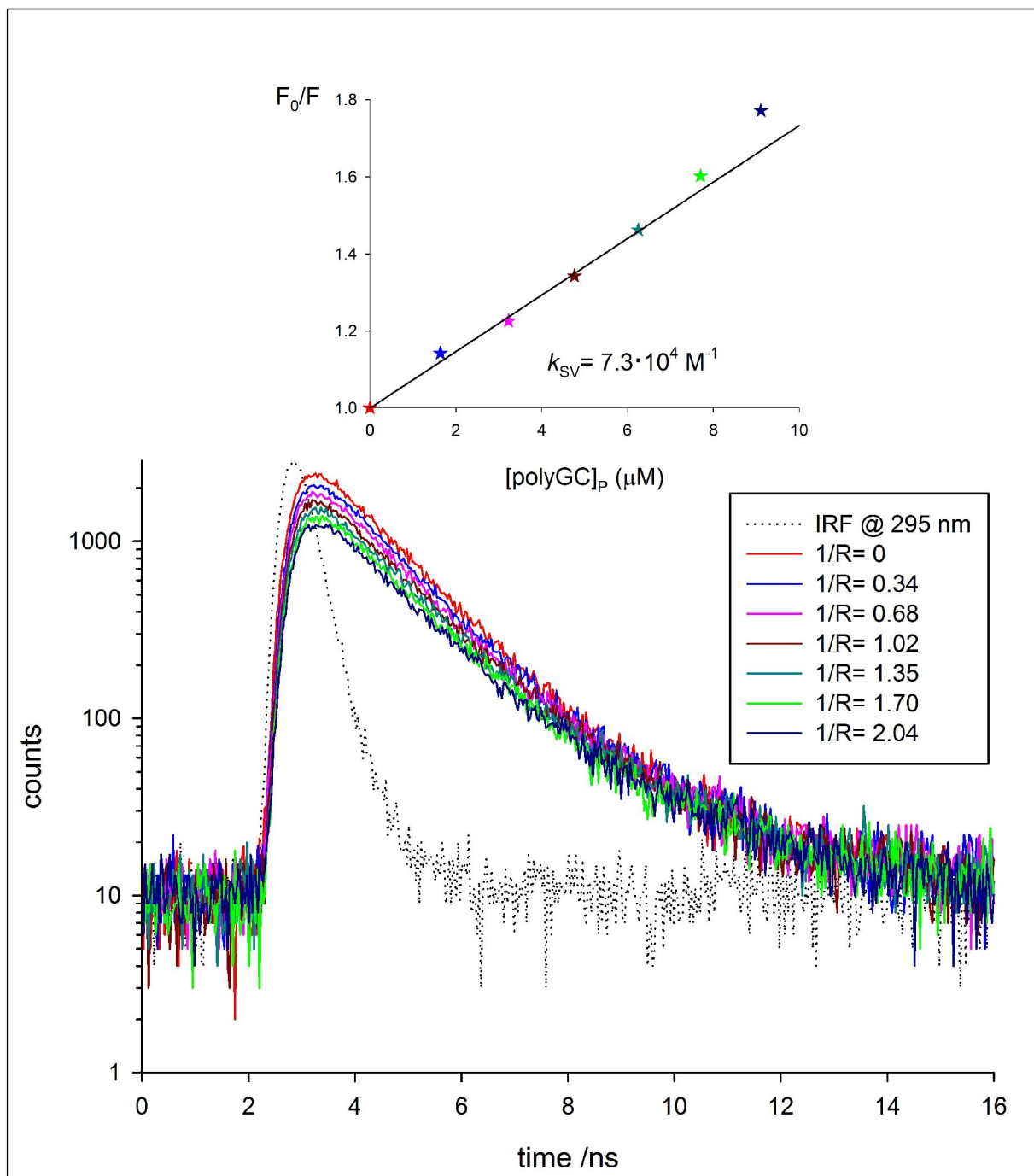
Fig. S8 Fluorescence lifetime measurements (TCSPC) for Cd(terpy)Cl$_2$ solution titrated with polyGC. R= [Cd(terpy)Cl$_2$]/[polyGC]$_P$; [Cd(terpy)Cl$_2$]= 4.3 μM in Tris 1 mM at pH= 7.5 - NaCl 2 mM; l= 1 cm; T= 298 K; λ_{ecc}= 295 nm; λ_{em}= 350 nm; ν_0= 10 MHz; acquisition time: 600 s. The inset shows the Stern-Volmer plot obtained from the TCSPC intensity data (colours as in the main graph).
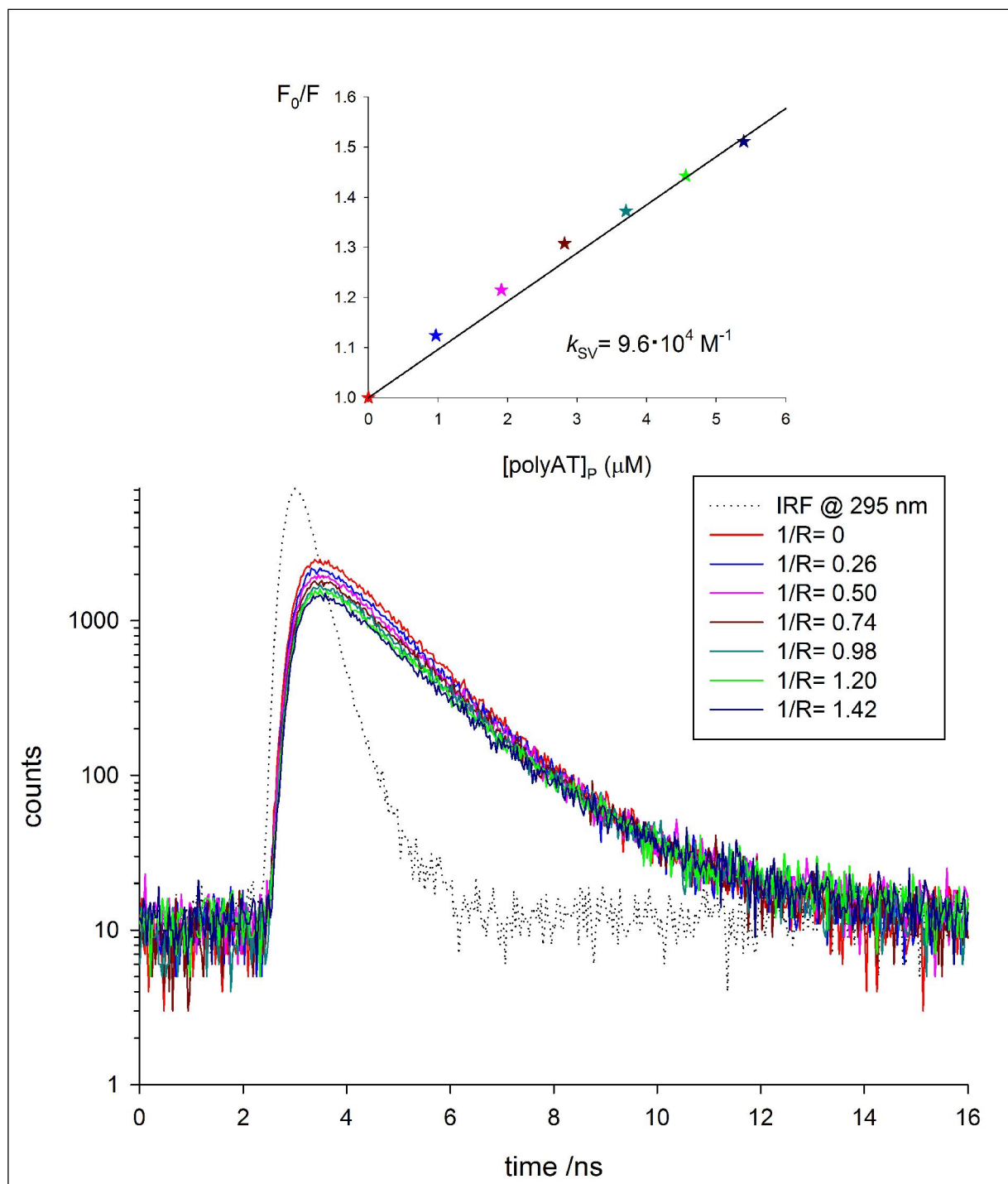
Fig. S9 Fluorescence lifetime measurements (TCSPC) for Cd(terpy)Cl$_2$ solution titrated with polyAT. R= [Cd(terpy)Cl$_2$]/[polyAT]$_P$; [Cd(terpy)Cl$_2$]= 3.8 μM in Tris 1 mM at pH= 7.5 - NaCl 2 mM; l= 1 cm; T= 298 K; λ_{ecc}= 295 nm; λ_{em}= 350 nm; ν_0= 10 MHz; acquisition time: 600 s. The inset shows the Stern-Volmer plot obtained from the TCSPC intensity data (colours as in the main graph).
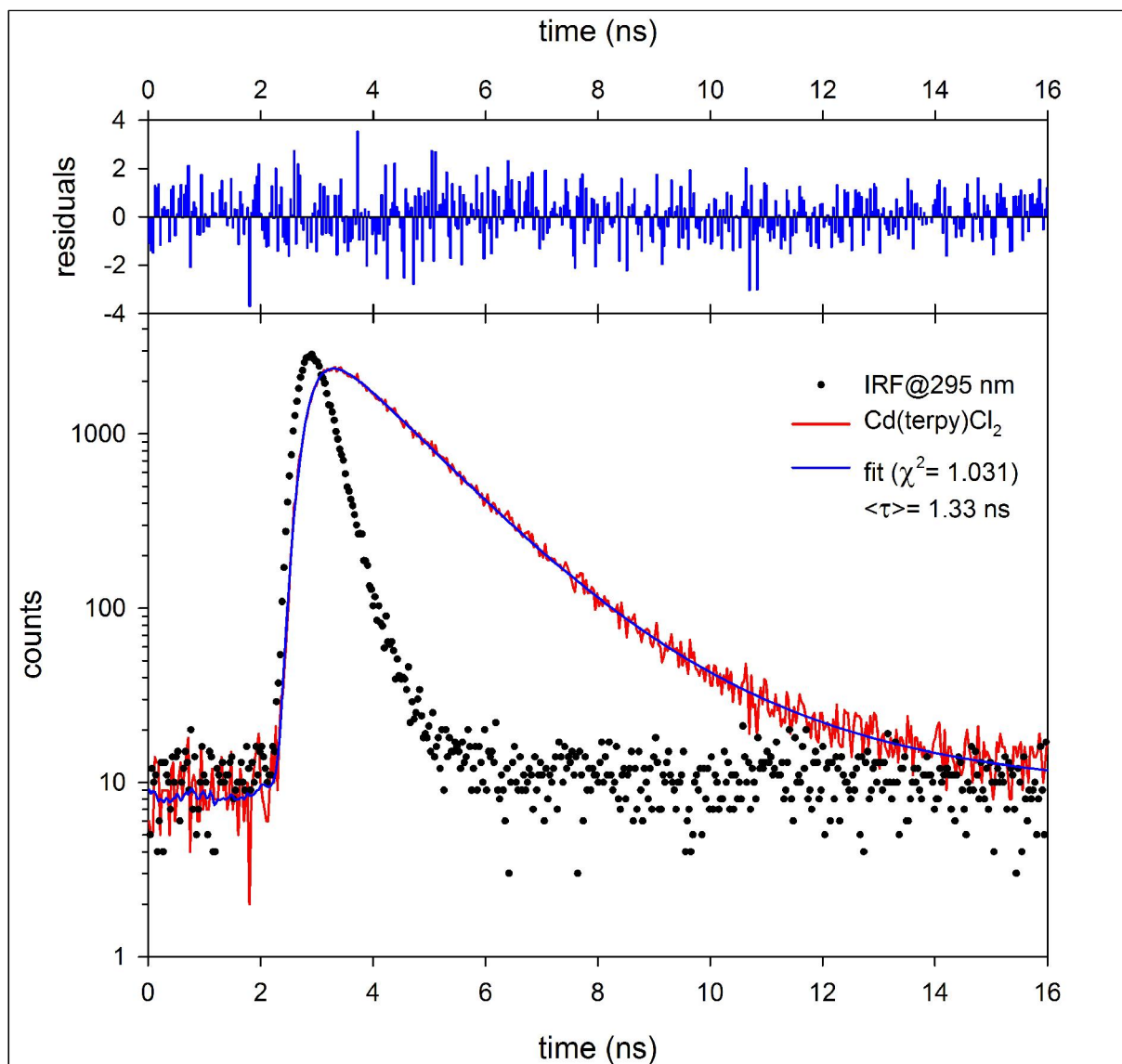
Fig. S10 Fluorescence lifetime measurements (TCSPC) for Cd(terpy)Cl$_2$ solution.

[Cd(terpy)Cl$_2$]= 4.3 µM in Tris 1 mM at pH= 7.5 - NaCl 2 mM; l= 1 cm; T= 298 K; λ_{ecc}= 295 nm; λ_{em}= 350 nm; ν_0= 10 MHz; acquisition time: 600 s.

The blue line in the main graph is the best fit according to a reconvolution equation between the IRF (dots) and the experimental decay (red line)

$$I(t) = \int_{-\infty}^{t} IRF(t') \sum_{i=1}^{n} A_i e^{-\frac{t-t'}{\tau_i}} dt'$$

The residuals are presented in the upper panel.

S.8. Supplementary data of QM/MM calculations

Table S4. DFT energy of the higher layer and extrapolated QM/MM energy (in Hartree) of the intercalation complexes of **1** with [dodeca(dA-dT)]$_2$ and [dodeca(dG-dC)]$_2$, and of **2** with [dodeca(dA-dT)]$_2$.

Model system	DFT Energy	QM/MM Energy
1/[dodeca(dA-dT)]$_2$	-2662.03620824	-2664.93283717
1/[dodeca(dG-dC)]$_2$	-2694.1640888	-2697.95923012
2/[dodeca(dA-dT)]$_2$	-2953.16053253	-2956.93816948

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