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Abstract
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A Rational Approach to Metal Loading of Organic Multi-Site Polymers: Illusion or Reality?**

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ABSTRACT

Since its identification as an independent topic after the first world war, the chemistry of (bio)polymers and macromolecules rapidly benefited from intense synthetic activities driven by contributors focussing on formulation and structural aspects. Satisfying rationalization and predictions concerning polymer organization, stability and reactivity were however delayed until the late fifties, when physical chemists set the basis of an adapted thermodynamic modelling. The recent emergence of metal-containing (bio)organic polymers (i.e. metallopolymers) thus corresponds to a logical extension of this field with the ultimate goal of combining the rich magnetic and optical properties of open-shell transition metals with the processability and structural variety of polymeric organic scaffolds. Since applications as energy storage materials, drug delivery vectors, shape-memory materials and photonic devices can be easily envisioned for these materials, the development of metallopolymers is faced to some urgency in producing novel exploitable structures, while the rational control of their formation, organization and transformation remains elusive. Caught between
the sometimes antagonistic requirements of economic efficiency on one side and of scientific
certainty on the other side, the ongoing achievements in the control of the metal loadings of multi-
site polymers are highlighted here with some tutorial discussions of luminescent lanthanidopolymers
as proof-of-concept.

1. Metallopolymers ‘driven and damaged’ by the attraction for structures, functions and
applications. At the turn of the 19th century, chemistry was simultaneously boosted by (i) major
advances in the modelling of energy changes (first Nobel prize in chemistry awarded to Jacobus
Henricus van’t Hoff in 1901 for the temperature dependence of chemical reaction and osmotic
pressure) and (ii) the identification of relationships between microscopic structures and macroscopic
properties (second Nobel prize in chemistry awarded to Hermann Emil Fischer in 1902 for the
synthesis, structural mapping and biological roles of sugars and purine). The contemporary atomic
revolution combined with the emergence of quantum mechanics deeply reinforced the microscopic
aspects and transformed chemistry into a structurally-inspired science for the next five to six decades.
In this context, the design and characterization of molecules with increasing complexities rapidly and
logically lead to the exploration of macromolecules and polymers.[1] The competition initiated after
the first world war between Meyer[2] and Staudinger[3] for synthesizing and characterizing
(bio)polymers only ended during the early fifties with the untimely death of the first during his
vacation (1952) and the awarding of the Nobel prize (1953) to the second. A complete directory of
synthetic methods and characterization processes are therefore at hand for the future generations,
together with a complete toolkit for identifying macromolecules and polymers in term of both
chemical structure and potential use in medicine and biology.[4] Although the statistical ratio of
polymerization (intermolecular binding) over macrocyclization (intramolecular binding) was
addressed by Kuhn’s theory during the thirties,[5] satisfying modelling of the energy changes which
drive polymerization[6] and polymer organizations[7] became available only after the end of the
synthetic battle. It is worth stressing here that, despite chemists being aware that matter
transformation and organization obey the following hierarchy: total entropy > free energy changes
structures, historical pathways in chemistry usually worked the other way round as exemplified by the design of novel molecules, macromolecules and polymers, which design usually preceded predictive thermodynamic approaches. The same story repeated itself during the early nineties with the emergence of supramolecular chemistry, which was characterized by the rapid production of a lot of extended structures corresponding to multi-component assemblies (helicates, cages, polyhedrons, clusters, knots, rotaxanes, see Fig. 1a for an illustration), while the original thermodynamic justifications for their formation required two decades for being critically approached, corrected and finally rationalized (see Fig. 1b for an illustration).

Figure 1 a) Assembly of a triple-stranded helicate erroneously claimed to be driven by positive cooperativity in 2005 and b) pertinent thermodynamic allosteric cooperativities reported in 2009. \( \Delta E_{\text{Luu}} = 0 \) corresponds to a statistical metal loading, whereas \( \Delta E_{\text{Luu}} < 0 \) and \( \Delta E_{\text{Luu}} > 0 \) stand for positive, respectively negative cooperative metal loadings (CH\(_3\)CN, 298 K).

It is therefore not so surprising that the field of metallopolymers, which relies on polymer chemistry and coordination chemistry, grew along the same guidelines with an original outburst of synthetic activities leading to a great deal of organic scaffolds flanked by various binding sites. Metal ions or metal complexes were then introduced either as independent guests (Wolf Type I and Wolf Type
II metallopolymers, Fig. 2b) or as part of the polymeric network (Wolf Type III metallopolymer, Fig. 2b). The last class of compounds, initially referred to as coordination polymers, are nowadays known as metal organic frameworks (MOFs) when some porous cavities can be identified within their infinite structures.\textsuperscript{[15]} Since the presence of open-shell transition metals brings novel optical and magnetic properties, which are unattainable with the rest of the main group (closed-shell) elements constituting the organic polymers, functional materials based on metallopolymers are actively explored and empirically optimized.\textsuperscript{[16]} Initial efforts for getting more insight into the organization and control of metallopolymers are indebted to Rehahn,\textsuperscript{[17]} who introduced a first structural classification based on metal-polymer interactions (Fig. 2a). An update and generalization using the standard metal-ligand bonding theory was proposed by Wolf few years later (Fig. 2b), and it was adopted by the community.\textsuperscript{[16a-b]}

**Figure 2** Classifications of metallopolymers according to a) Rehahn\textsuperscript{[17]} and b) Wolf.\textsuperscript{[16a-b]}
As the thermodynamic modelling of the formation of main group (bio)polymers is already challenging,[6],[7] the consideration of additional (supra)molecular interactions occurring between the polymeric backbone and d-block cations in metallopolymers, or versatile 4f-block cations in lanthanidopolymers, are far beyond the possibilities of current theoretical treatment and predictions.[18] The situation becomes even more complicated with the use of copolymers, in which the polymeric fragments bearing the bound metal coexist with non-coordinating bridging units (right-part of Fig. 3).

![Partition of a sample of 158 lanthanidopolymers within the frame of Wolf’s classification.[16a-b]](image)

**Figure 3** Partition of a sample of 158 lanthanidopolymers within the frame of Wolf’s classification.[16a-b]

Considering a sample of 158 metallopolymers that incorporate trivalent lanthanoid cations, Ln$^{3+}$, as active metallic centers (i.e. lanthanidopolymers),[19] 40% belongs to Wolf Type III metallopolymers, the structures of which are accessible by X-ray diffraction analysis. The metal loading in these compounds is trivial since no metal exchange process can be addressed beyond statistical doping (blue sector in Fig. 3).[20] Among the remaining 60% of lanthanidopolymers assigned to Wolf Type I and II (green + red sectors in Fig. 3) and which are prone to undergo addressable and reversible metal-
polymer associations/dissociations, only about one third (22%) corresponds to organized homopolymers or copolymers (red sectors in Fig. 3). Among these candidates, we are aware of a single attempt, which proposes a comprehensive and predictive thermodynamic model for addressing metal loading.\[21\] By contrast, the vast majority of Wolf Type I and II lanthanidopolymers collected in Fig. 3 have been carefully studied for quantifying their optical\[14b,16d\] and magnetic\[22\] properties, the dependence of which on external stimuli (pressure, temperature, solvent, stoichiometry, analyte) is at the origin of the design of multi-responsive and multi-stimuli materials.\[23\] Wolf Type I and Type II metallopolymers would thus greatly benefit from a predictive, rational and organized loading of open-shell metal ions, an approach currently strictly limited to polymeric backbones incorporating inert preformed Ru\textsuperscript{II} and Os\textsuperscript{II} complexes.\[14\] The alternative labile metallic centers are currently (under)exploited as versatile partners, and this despite their crucial contributions to the desired properties of the final materials.

2. The site-binding model as a guide for rationalizing thermodynamic metal loading in metallopolymers. The thermodynamic modelling of the fixation of a single metallic cation (i.e. the guest: M) to a single binding site (i.e. the host: L) according to equilibrium (1), where
\[
\beta_{1,1}^{ML} = \exp\left(-\Delta G_{1,1}^{ML} / RT\right)
\]
is the unitless 1:1 host-guest association constant, is as old as coordination chemistry. Its transposition into the field of metallopolymers in equilibrium (2) seems rather trivial according that (i) an adequate statistical scheme is applied for taking care of the large number of \(N\) available sites in the polymer \(P\) for accommodating the \(m\) entering metals \((m \leq N)\) and (ii) the intrinsic metal-binding site affinity \(f_{j}^{M,P}\) characterizing a single host-guest interaction (a concept closely related to \(\beta_{1,1}^{ML}\)) can be modulated by the considerable number of intermetallic (i.e. guest-guest) interactions (Fig. 4a).\[24\]

\[
\begin{align*}
\text{L} & + \text{M} \underset{\text{[LM]}}{\rightleftharpoons} \\
\text{P} & + \text{mM} \underset{\text{[PM}_m\text{]}}{\rightleftharpoons} \\
\Delta G_{1,1}^{ML} &= -RT \ln \left(\beta_{1,1}^{ML}\right) \quad (1) \\
\Delta G_{m,1}^{MP} &= -RT \ln \left(\beta_{m,1}^{MP}\right) \quad (2)
\end{align*}
\]
In terms of statistical mechanics, the relevant information on the binding properties of M to P is contained in the semi-grand canonical partition function $\Xi$.\cite{25} The latter can be expanded in terms of the metal activities $a_M$ and one obtains the so-called binding polynomial (left part of eq. 3).

$$\Xi = \sum_{n=0}^{N} \beta_{n,i} (a_M)^n = \bar{V}_i T^N V_g$$

This barbaric function $\Xi$ may frighten non-specialists, but its consideration is only justified in this minireview since its derivative (left part of eq. 4) is the key concept, which correlates thermodynamic stability constants with the experimental degree of metalation $\theta_m = \langle m \rangle / N$, also known in

**Figure 4**

a) Thermodynamic model for the successive intermolecular connections of guests (M) to a one-dimensional multi-site polymer (P). $\Delta G_{\text{aff}}^{M,P} = -RT \ln (f_i^{M,P})$ is the free energy of intermolecular metal-binding site affinity and $\Delta E_{i,j}^{M,M} = -RT \ln (u_{i,j}^{M,M})$ is the free energy of intermetallic interaction. b) Transfer matrix $T$ adapted to metal loading limited to nearest-neighbour intermetallic interactions.\cite{25,26} c) Semi-grand canonical partition function $\Xi$ computed with eq. 3 for the tetranuclear helicate shown in Fig. 1a. Cartoons of each microspecies contributing to the macroscopic constants $\beta_{n,i}^{M,P}$ are shown on the right.
coordination chemistry as the occupancy factor estimating the average of bound metals per available sites in the receptor (right part of eq. 4).

$$\theta_m = \frac{\langle m \rangle}{N} = 1 \sum_{n=0}^{N} m p_{m,1}^{M,P} (a_m)^n = 1 \sum_{n=0}^{N} \beta_{m,1}^{M,P} (a_m)^n$$

Reasonably assuming that the molar concentration of free metal $|M|$ can be taken as a good estimation of its activity ($a_m = \gamma_m |M| = |M|$), the experimental determination of the occupancy factor $\theta_m$ for a series of solutions with different $|M_n|, |P_n|$ pairs (for instance during the NMR titration of a solution of polymer $P$ with increasing amounts of metallic salts) allows the determination of free metal concentrations $|M|$ for each mixture (eq. 4, right part). Plots of $\theta_m$ as a function of $|M|$ (or log$|M|$) are known as binding isotherms (Fig. 5). They can be fitted with the help of non-linear least-square methods to the derivative of the partition function $\beta_{m,1}^{M,P}$ shown in the center of eq. 4) in order to extract a set of $N$ macroscopic association constants $\beta_{m,1}^{M,P}$. The ultimate modelling of the latter constants with the resort of only two basic parameters: (1) the intrinsic metal-binding site affinity $f_{i}^{M,P}$ and (2) the intermetallic interaction parameter $u_{i,j}^{M,M}$ (see Fig. 4a) exploits the cluster expansion technique, which relies on transfer matrix formalism (right part of eq. 3). $V_g = (1 \ 0 \ ...)$ is the (transposed) generating vector of dimension $p$ initiating the effect of the square $p \times p$ transfer matrix $T$, which takes into account the change produced in the partition vector when the subchain is extended by one elementary unit on the left (see Fig. 4b). $V_t = (1 \ 1 \ ...)$ is the transposed terminating vector, also of dimension $p$.[26] Further justifications for this procedure are beyond the scope of this tutorial review and the interested reader may find more details in references [25] and [26]. It is sufficient to note here that if (i) one considers a unique metal-site affinity $f_{i}^{M,P}$ for any binding units along the receptor and (ii) one limits the intersite pair interactions to nearest-neighbours as expressed by the Boltzmann factor $u_{i,j}^{M,M} = \exp (-\Delta E_{i,j}^{M,M}/RT)$, the square 2x2 transfer matrix $T$
depicted in Fig 4b is pertinent for building the semi-grand partition function $\Xi$ of any linear metallo-polymer $P^N$ shown in Fig. 4a.

**Figure 5**  
(a-b) Binding isotherms (full traces) computed for the metal loading of the oligomeric host scaffold $P^N$ depicted in Figure 1a and in which a maximum of $N = 4$ metals can be bound. Part a) highlights variable metal-binding site affinities for fixed $\Delta E_{1,2}^{MM} = 0$ and part b) shows variable nearest neighbor interactions for fixed $\Delta G_{aff}^{MM} = -40$ kJ/mol (the dashed trace displays the binding isotherm for an infinite polymer ($N \rightarrow \infty$) with $\Delta E_{1,2}^{MM} = 10$ kJ/mol). c) Dominant microspecies predicted for half-filled infinite polymers ($\theta_n = 0.5$) upon the operation of positive (top), zero (middle) or negative (bottom) cooperativity.
Assuming that the helicate depicted in Fig. 1a corresponds to a linear oligomeric host scaffold \( P^{N=4} \) formed by the three wrapped strands, to which a maximum of four lanthanoid cations can be bound, the calculation of the appropriate partition function 
\[
\Xi = \sum_{n=0}^{4} \beta_{n,1}^{M,P} (a_{M}^{m}) = V_{i} T^{d} V_{g}
\]
tutorially illustrated in Fig. 4c. It leads to a complete modelling of each macroscopic constant \( \beta_{n,1}^{M,P} \) with the help of only two microscopic descriptors \( f_{1}^{M,P} \) and \( u_{i-2}^{MM} \). With the site-binding model in hand, the locations (Fig 5a) and shapes (Fig. 5b) of the experimental binding isotherms can be analyzed as direct estimations for the intrinsic affinities 
\[
\Delta G_{i}^{M,P} = -RT \ln \left( f_{i}^{M,P} \right)
\]
and the intermetallic interactions 
\[
\Delta E_{i-2}^{MM} = -RT \ln \left( u_{i-2}^{MM} \right)
\]
respectively. Moreover, the organization of the metal loading along the linear polymeric chain is controlled by the allosteric cooperativity factors 
\[
u_{i-2}^{MM} = \exp \left( -\Delta E_{i-2}^{MM} / RT \right)
\]
leading either to pure statistical distribution \( (u_{i-2}^{MM} = 1, \text{no cooperativity, Fig. 5c middle}) \), metal clustering \( (u_{i-2}^{MM} > 1, \text{positive cooperativity, Fig. 5c top}) \) or metal alternation \( (u_{i-2}^{MM} < 1, \text{negative cooperativity, Fig. 5c bottom}) \).


Prior to embarking on the delicate synthesis of monodisperse linear multi-site polymeric receptors, it is prudent to first identify a well-behaved host/guest pair, the association process of which is not complicated by competitive and/or parasitic reactions. Taking the semi-rigid tridentate ligand \( L_{1} \) (N\(_2\)O donor unit) and \( L_{2} \) (N\(_3\) donor unit) as elementary binding units, their reactions with \([\text{Ln(NO}_3\text{)}_3(\text{H}_2\text{O})]\) and \([\text{Ln(hfa)}_3(\text{dig})]\) lanthanoid containers (hfa = 1,1,1,5,5,5-hexafluoro-2,4-pentanedione and dig = bis(2-methoxyethyl) ether) indeed show similar host-guest affinities \((-33 \leq \Delta G_{i,1}^{\text{EuX}_1,L_{1,4}} \leq -25 \text{ kJ/mol in acetonitrile})\), but only the formation of the complex \{\( L_{1}[\text{Ln(NO}_3\text{)}_3]\)\} matches the requirement for the operation of an above-mentioned well-behaved host/guest pair association (Fig. 6, left).\(^{[27]}\)
However, \( \textbf{L1} \) is unsymmetrical and an organized linear polymer made of a series of \( \text{N}_2\text{O} \) binding is difficult to synthesize. Returning to the symmetrical ligand \( \textbf{L2} \), the complex \( \{\textbf{L2}[\text{Ln(hfa)}_3]\} \) is the next most promising candidate, according that the embarrassing ligand double-exchange process leading to the ionic pair \( [\text{Ln(\textbf{L2})}_2(\text{hfa})_2]^{+}/[\text{Ln(hfa)}_4]^- \) can be blocked (Fig. 6, right). This condition is met in dichloromethane because the solvation of polar systems is severely reduced in solvents with low dielectric constants.\(^{[21a]}\) The conditional association reactions between the lipophilic ligand \( \textbf{L3} \), an analogue of \( \textbf{L2} \), and \( [\text{Ln(hfa)}_3] \) guests performed in \( \text{CD}_2\text{Cl}_2 + 0.14 \text{ M dig} \) (Fig. 7a) thus provide ‘well-educated’ binding isotherms, which can be conveniently fitted to equilibrium 1 (Fig. 7b).\(^{[21a]}\) Suzuki-based strategies lead to the synthesis of three linear organic polymers with acceptable polydispersities indexes (1.13 ≤ DPI ≤ 1.25)\(^{[21b]}\) and which incorporate approximately ten \( (\textbf{P3}^{\text{N=12}}) \), twenty \( (\textbf{P3}^{\text{N=20}}) \) and thirty \( (\textbf{P3}^{\text{N=31}}) \) tridentate elementary \( \textbf{L3c} \) units, where the bridging phenyl rings were decorated with hexyloxy chains for solubility reasons (\( R = \text{C}_6\text{H}_{13} \) in Fig. 8a, left).
Figure 7  Occupancy factors and binding isotherms deduced from $^1$H NMR titration of $L_3$ with $[\text{Ln(hfac)}_3\text{(dig)}]$ ($\triangle = \text{La}, \bullet = \text{Eu}, \blacksquare = \text{Y}$) in CD$_2$Cl$_2$ + 0.14 M dig at 293 K. The dotted lines correspond to the fitted curves computed with eq. 4 and using $\beta_1^{\text{Ln(hfa)},L_3}$ gathered in the figure. Adapted from ref. [21a].

Reactions between $P_3$ and $[\text{Ln(hfa)}_3]$ guests provided binding isotherms with variable locations and shapes (Fig. 8a). For polymers with polydispersity indexes smaller than 1.30, the binding isotherms can be conveniently reproduced using eqs 3-4 and $\langle N \rangle$ derived from the weight average molecular weight. The metal-site affinities $\Delta G_{N_j}^{\text{Ln,P}3^V} = -RT \ln \left( \frac{\text{f}_{N_j}^{\text{Ln,P}3^V}}{N_j} \right)$ and intersite pair interactions $\Delta E_{i,j}^{1n,1n} = -RT \ln \left( \frac{1}{n_{i,j}^{1n,1n}} \right)$ collected in Fig. 8b result from this procedure.$^{[21b]}$ When polydispersity indexes are larger than 1.30, a Gaussian deconvolution of the size extrusion chromatogram (SEC) provides a set of individual oligomers together with their specific mole fractions, which represents the speciation in solution. The adaptation of eqs 3 and 4 for this situation is beyond the scope of this minireview, but details for a study case, where DPI = 1.33, can be found in reference [21a].
Figure 8  a) Occupancy factors and binding isotherms deduced from $^1$H NMR titrations of polymers $\text{P3}^N$ ($R = C_6H_{13}$) with $[\text{Ln(hfac)}_3(\text{dig})]$ ($\blacktriangle = \text{La}$, $\bullet = \text{Eu}$, $\blacksquare = \text{Y}$) in CD$_2$Cl$_2 + 0.14$ M dig at 293 K and b) pertinent metal-site affinities $\Delta G_{\text{N}_i}^{\text{Ln,P3}^N}$ and intersite pair interactions $\Delta E_{i-2}^{\text{Ln,Ln}} = -RT \ln \left( \frac{1}{N_i} \right)$ deduced with eqs 3-4 ($R_{\text{La}}^{\text{CN}=9}$ is the nine-coordinate lanthanoid radius). Adapted from ref. [21b].

Beyond the surprising 30% decrease of the intrinsic affinity in going from the monomer $\text{L3}$ (-17 ≤ $\Delta G_{\text{N}_i}^{\text{Ln,L3}} = -RT \ln \left( \frac{1}{N_i} \right)$ ≤ -13 kJ/mol, Fig. 7) to any of the polymers $\text{P3}^N$ (-12 ≤ $\Delta G_{\text{N}_i}^{\text{Ln,P3}^N}$ ≤ -8 kJ/mol, Fig. 8b), a trend which will be addressed in the next section, it appears that both intrinsic
affinities and intermetallic interactions depend on the choice of the metal, whereas the length of the polymeric chain has little (if any) influence. Despite the common belief that the number of repeating units (i.e. the length) in rigid polymer affects the final properties, a claim fully justified when discussing viscosities or diffusion coefficients for instance, there is no obvious reason for inducing significant changes in intermolecular association processes. The slightly concave distribution of the host-guest affinities (Fig. 8b, left part) mirrors that found in the monomer L3 (Fig. 7b), a phenomenon produced by the increased bulk of the metallic coordination sphere induced by lanthanoid contraction along the series.[21a]

Figure 9  a) Thermodynamic Born-Haber cycle for the addition of the \((m+1)\) [Ln(hfa)₃] lanthanoid container, characterized by the \(K_{m+1}\) successive stability constant, to the lanthanidopolymer \{P₃\}[Ln(hfa)₃] \(m\}. b) Hydrodynamic diameters of the lanthanidopolymers \{P₃\}[Ln(hfa)₃] \(m\} as a function of the occupancy factor \(\theta\) for lanthanoid loadings (CH₂Cl₂ + 0.15 mol·dm⁻³ at 293K). Adapted from ref. [21b].
Catching the origin of the ever-increasing positive allosteric cooperativity (i.e. \( \Delta E_{1 \rightarrow 2}^{\text{Ln,Ln}} = -RT \ln \left( \frac{1}{n_{1,2}} \right) < 0 \)) observed along the lanthanoids series (Fig. 8b, right part) is more challenging. It can be approached with the help of the Born-Haber cycle depicted in Fig. 9a, which is summarized in eq. (5)\[12b\]

\[
\Delta G_{K_{m+1}, \text{sol}}^0 = \Delta G_{K_{m+1}, \text{gas}}^0 - \Delta_{\text{solv}} G_{P3\text{Ln},n}^0 - \Delta_{\text{solv}} G_{\text{Ln}}^0 + \Delta_{\text{solv}} G_{P3\text{Ln,n}}^{0} \tag{5}
\]

The selected complexation process refers to the addition of one lanthanoid container \([\text{Ln(hfa)}_3]^{m+}\) to the \(\{P3^N[\text{Ln(hfa)}_3]_m\}\) microspecies to give \(\{P3^N[\text{Ln(hfa)}_3]_{m+1}\}\). The application of the site-binding model (eq. 3) for estimating the \(K_{m+1}\) successive stability microconstant in the gas phase leads to

\[
\Delta G_{K_{m+1}, \text{gas}}^0 = -RT \ln \left( f_{i,\text{gas}}^{\text{Ln}} \right) + \Delta E_{1 \rightarrow 2, \text{gas}}^{\text{Ln,Ln}} .
\]

With this in mind, eq. (5) transforms into eq. (6)\[21b\] when the various solvation energies \(\Delta_{\text{solv}} G^0\) are modelled with the Onsager equation (\(\mu\) are the electric dipole moments and \(R_H\) are the hydrodynamic radii of the species considered in Fig. 9a).\[28\]

\[
\Delta E_{1 \rightarrow 2, \text{sol}}^{\text{Ln,Ln}} = \Delta E_{1 \rightarrow 2, \text{gas}}^{\text{Ln,Ln}} + RT \ln \left( \frac{f_{i,\text{gas}}^{\text{Ln}}}{f_{i,\text{sol}}^{\text{Ln}}} \right) + \frac{N_{av}}{4\pi \varepsilon_0} \left( \varepsilon_r - \frac{1}{2\varepsilon_r + 1} \right) \left[ \frac{\mu_{\text{Ln}}^2}{(R_{H,\text{Ln}})^3} + \frac{\mu_{P3\text{Ln,n}}^2}{(R_{H,P3\text{Ln,n}})^3} - \frac{\mu_{P3\text{Ln,n}}^2}{(R_{H,P3\text{Ln,n}})^3} \right] \tag{6}
\]

The first contribution in eq. (6) corresponds to the gas-phase intermetallic interaction \(\Delta E_{1 \rightarrow 2, \text{gas}}^{\text{Ln,Ln}}\), which amounts to less than 0.5 kJ/mol in \(\{P3^N[\text{Ln(hfa)}_3]_{m+1}\}\), this whatever the selected lanthanoid.\[29\] Since the ratio \(\frac{f_{i,\text{gas}}^{\text{Ln}}}{f_{i,\text{sol}}^{\text{Ln}}}\) can be reasonably taken as constant along the lanthanoid series for a given receptor,\[21b\] any modulation of \(\Delta E_{1 \rightarrow 2, \text{sol}}^{\text{Ln,Ln}}\) reflects the balance of the solvation energies. The first player \(\frac{\mu_{\text{Ln}}^2}{(R_{H,\text{Ln}})^3}\) refers to \(\Delta_{\text{solv}} G_{\text{Ln}}^0\), for which the faint dipole moment computed for \([\text{Ln(hfa)}_3] (\mu_{\text{Ln}} \leq 0.5\ \text{Debye})[30]\) makes it negligible. Consequently, the two last terms of eq. (6) are responsible for the variation of \(\Delta E_{1 \rightarrow 2, \text{sol}}^{\text{Ln,Ln}}\) depicted in Fig. 8b (right). Dynamic light scattering data recorded upon titration of \(P3^N\) with \([\text{Ln(hfa)}_3]_{\text{dig}}\) in dichloromethane (Fig. 9b) show that the hydrodynamic diameters \(d_{H} = 2R_{H,P3\text{Ln,n}}\) of the lanthanidopolymer \(\{P3^N[\text{Ln(hfa)}_3]_m\}\) globally increases upon loading with \(\text{Ln} = \text{La}\) (Fig. 9b, left). The two crucial terms \(\left[ \frac{\mu_{P3\text{Ln,n}}^2}{(R_{H,P3\text{Ln,n}})^3} - \frac{\mu_{P3\text{Ln,n}}^2}{(R_{H,P3\text{Ln,n}})^3} \right] \) in eq. (6) thus
correspond to a very limited contribution to $\Delta E_{1-2,\text{sol}}$ since $R_{H,P3L_{n}} < R_{H,P3L_{n+1}}$, whereas $\mu_{H,P3L_{n}}^{2} \leq \mu_{H,P3L_{n+1}}^{2}$.\textsuperscript{[21b]} The opposite contractions of the hydrodynamic radii observed upon metal loading with Ln = Eu and especially with Ln = Y (Fig. 9b, right) provide negative $\left[\mu_{H,P3L_{n}}^{2} / (R_{H,P3L_{n}}^{3}) - \mu_{H,P3L_{n+1}}^{2} / (R_{H,P3L_{n+1}}^{3})\right]$ contributions in eq. (6) because $R_{H,P3L_{n}} > R_{H,P3L_{n+1}}$ whilst $\mu_{H,P3L_{n}}^{2} \leq \mu_{H,P3L_{n+1}}^{2}$ is retained. This reinforces negative cooperativity for the loading with heavier lanthanoids, a trend in agreement with the experimental data: $0 \approx \Delta E_{1-2,\text{sol}}^{\text{La,La}} > \Delta E_{1-2,\text{sol}}^{\text{Eu,Eu}} > \Delta E_{1-2,\text{sol}}^{\text{Y,Y}}$ (Fig. 8b).

4. Thermodynamic optimization of metal loading: shortcutting polymers with dimers. The two crucial thermodynamic parameters characterizing the metal loading of a linear polymer, $\Delta G_{i}^{\text{M,P}} = -RT \ln \left(f_{i}^{\text{M,P}}\right)$ and $\Delta E_{i-2}^{\text{M,M}} = -RT \ln \left(u_{i-2}^{\text{M,M}}\right)$ are also accessible via the titration of simple model dimers D since the fixation of the first metal to give the unsaturated mononuclear complex [DM] defines $f_{1}^{\text{M,P}} = \beta_{1,1}^{\text{M,D}} / 2$ (eq. 7), while any deviation from statistics in the saturated dinuclear complex [DM$_{2}$] yields an estimate of the intermetallic interaction $u_{i-2}^{\text{M,M}} = \beta_{2,1}^{\text{M,D}} / 4 \left(\beta_{1,1}^{\text{M,D}}\right)^{2}$ (eq. 8).

\[
\begin{align*}
\text{D} + \text{M} & \underset{\text{[DM]}}{\rightleftharpoons} f_{1}^{\text{M,D}} = \beta_{1,1}^{\text{M,D}} / 2 \\
\text{D} + 2 \text{M} & \underset{\text{[DM$_{2}$]}}{\rightleftharpoons} \beta_{2,1}^{\text{M,D}} = \left(f_{1}^{\text{M,D}}\right)^{2} u_{1-2}^{\text{M,M}}
\end{align*}
\] (7) (8)

With this in mind, the influence of various geometries imposed by the dihexyloxy-phenyl bridges (ortho-meta-para) implemented in the dimers D1-D3 (Fig. 10a) on the metal loading could be explored with much less synthetic efforts compared with those required for extracting the same information using related polymers.\textsuperscript{[29]} A large number of different lanthanoids were thus investigated prior to conclude that the best compromise between interligand interactions and metallic size did not depend on the relative orientation of the successive binding units in the dimers since the same optimum was systematically reached around Ln = Er (Fig. 10b, top). On the contrary, the intermetallic interaction $\Delta E_{1-2}^{\text{M,M}}$ is modulated by the relative orientation of the successive binding sites (Fig. 10b,
bottom). The latter trend can be approached by a Born-Haber cycle similar to that built in Fig. 9a (eq. 6). Rough theoretical calculations\(^{29}\) predict \(\Delta E_{1-2}^{L_{a}L_{a}} (D3) = -7.3 \text{ kJ/mol} < \Delta E_{1-2}^{L_{a}L_{a}} (D1) = 2.0 \text{ kJ/mol} < \Delta E_{1-2}^{L_{a}L_{a}} (D2) = 12.2 \text{ kJ/mol}\), a relative order in line with the experimental progression highlighted in Fig. 10b.\(^{29}\)

![Molecular structures of \{Dk[Ln(hfa)\(_3\)]\(_2\}\} dimers found in their associated crystal structures and b) associated intrinsic host-guest affinities \(\Delta G_{N_{a}}^{L_{a}Dk}\) and intersite interactions \(\Delta E_{1-2}^{L_{a}L_{a}} = -RT \ln \left( I_{N_{a}}^{L_{a}Dk} \right)\) for the loading of ligands \(L_3\) (magenta), \(D1\) (red), \(D2\) (green), and \(D3\) (blue) with [Ln(hfa)\(_3\)(dig)] \(\left( \frac{1}{R_{CN-9}} \text{ is the inverse of nine-coordinate lanthanoid radii, CD}_{2}\text{Cl}_2 + 0.14 \text{ M dig, 298 K.} \right)\).\(^{29}\)

Altogether, the experimental magnitude \(-2 \leq \Delta E_{1-2}^{M_{M}} \leq +2 \text{ kJ/mol}\) found in \{Dk[Ln(hfa)\(_3\)]\(_2\}\} does not deviate sufficiently from thermal energy at room temperature \((RT = 2.5 \text{ kJ/mol})\) for inducing any specific metal ordering along the linear polymeric chain. The situation changes when unsymmetrical beta-diketonate lanthanoid containers [Ln(pbta)\(_3\)] are used as guests because an unprecedented
anticooperative process twice as large as thermal energy can be evidenced in \{D2[Ln(pbta)3]2\} (blue trace in Fig. 11). The latter beneficial effect paves the way for the programming of metal alternation along one dimension.

Figure 11  a) Loading of the dimer D2 with lanthanoid containers LnX3 and b) associated occupancy factors and binding isotherms built from NMR titrations of D2 with [Eu(hfa)3]dig (symmetrical container X = hfa: red disks) and [Eu(pbta)3]dig (unsymmetrical container X = pbta: blue triangles for 1H NMR and blue crosses for 19F NMR) in CD2Cl2 + 0.14 M dig at 298 K. The dotted traces correspond to the fitted curves computed with eqs 3-4 and using \(\Delta G_{N_3}^{\text{EuX}}\) and \(\Delta E_{N_2-1}^{\text{EuX}}\) collected in the picture.

A second surprise arose with the discovery of an exponential decrease of the intrinsic affinity \(J_{N_3}^{\text{Ln,Py}}\) with the length \(N\) of the linear polymer (Fig. 12a). Again sovaltion effects considered in a judicious Born-Haber cycle (Fig. 12b and eq. 9) saved the day. The application of the site-binding model combined with Kuhn theory of shape persistence and Onsager equation eventually transforms eq. 9 into eq. 10, where \(\beta\) is a measure of the rigidification of the polymeric strand induced by metal complexation.
\begin{equation}
\Delta G_{\text{exch, gas}}^{L3 \rightarrow P3^y} - \Delta G_{\text{exch, sol}}^{L3 \rightarrow P3^y} = \Delta_{\text{solv}} G_0^{L3} - \Delta_{\text{solv}} G_0^{P3^y} + \frac{\Delta_{\text{sub}} G_0^{P3^y}}{n_{\text{Ln}}} - \Delta_{\text{sub}} G_0^{L3_{\text{Ln}}}
\end{equation}

\begin{equation}
N_{N, \text{sol}} \cdot e^{-
\left[
\left(
\Delta_{\text{sub}} G_0^{L3} - \Delta_{\text{sub}} G_0^{P3^y} + \Delta_{\text{sub}} G_0^{P3^y} - \Delta_{\text{sub}} G_0^{L3_{\text{Ln}}}
\right)/RT
\right]} \cong N_{N, \text{sol}} \cdot N_{L3}^{\beta_{\text{sub}} G_0^{L3}/RT}
\end{equation}

The power law dependence of the intrinsic host-guest affinity on the number of binding site (eq. 10, right) prevents the use of the monomer L₃ as a valuable single-site-binding reference for analyzing any deviations from statistics operating in polymeric receptors. In other words, the common method, which exploits the binding affinity measured separately in the monomer as the basis for extracting cooperative contributions occurring in multi-site receptors is globally erroneous for any multiple intermolecular association process, and this despite its very large dissemination in biology, pharmacy and medicine.

**Figure 12**

a) Intrinsic affinity parameters $f_{N_{i, \text{sol}}}^{Y,P3^y}$ for the loading of ligands L₃ ($N = 1$), D₁ ($N = 2$) and P₃$^N$ ($N = 10, 12, 20, 31$) with [Y(hfa)₃] ($N$ is the number of available tridentate binding sites, CD₂Cl₂ + 0.14 M dig, 298 K). The dotted trace was fitted with eq. 10. b) Thermodynamic cycle for ligand exchange around a [Ln(hfa)₃] container.[29]

Being concerned by some inadequate approaches and approximations used since decades for tentatively analyzing allosteric cooperativity factors characterizing multivalent (bio)chemical receptors, we first critically questioned the consequences of our own choice to fix the concentration of diglyme co-ligand at 0.14 M. This condition is expressly required for transforming the ligand.
exchange process shown in Fig. 7a (eq. 11) into a simple association process (eq. 12) compatible with its analysis with the help of the site-binding model (eqs 1-4).[34]

\[
\text{L3} + [\text{Ln(hfa)}_3\text{dig}] \rightleftharpoons \{\text{L3}[\text{Ln(hfa)}_3]\} + \text{dig}
\]

\[K_{1,1,\text{exch}}^{\text{Ln(hfa)},0.3}\] (11)

\[
\text{L3} + [\text{Ln(hfa)}_3] \rightleftharpoons \{\text{L3}[\text{Ln(hfa)}_3]\}
\]

\[\beta_{1,1}^{\text{Ln(hfa)},0.3}\] (12)

Repeating the titration of the monomeric ligand L3 with [Ln(hfa)_3] in pure dichloromethane (without added diglyme) indeed showed that the quotient of reaction

\[Q_{1,1,\text{exch}}^{\text{Ln(hfa)},0.3} = \frac{[\text{L3}[\text{Ln(hfa)}_3]]}{[\text{L3}][\text{Ln(hfa)}_3]} \]

, usually (but erroneously) taken as the thermodynamic constant \[K_{1,1,\text{exch}}^{\text{Ln(hfa)},0.3}\] (eq. 11),[35] indeed exponentially depends on the equilibrium concentration of the formed complex (Fig. 13a).[34]

**Figure 13** a) Dependence of the quotient of reaction at equilibrium \(Q_{1,1,\text{exch}}^{\text{Ln(hfa)},0.3}\) with the progress of the exchange reaction (eq. 11) and b) highlight of the thermodynamic free energy changes \(\Delta G_{1,1,\text{exch}}^{\text{Ln(hfa)},0.3}\) according to eq. 13.[35]
This intriguing behavior could be assigned to the change in activity coefficients induced by the disruption of the chemical potential of the solvent accompanying the metal loading.\cite{34} A correction of the law of mass action is required in eq. (13) where $c^0$ is the standard concentration of the reference state.\cite{35}

$$-RT \ln \left( K_{1,1,\text{exch}}^{\text{Ln(hfa)},1,3} \right) = -RT \ln \left( K_{1,1,\text{exch}}^{\text{Ln(hfa)},1,3} \right) + \left( \left[ \left[ \text{L}3 \left[ \ln \left( \text{hfa} \right) \right] \right] / c^0 \right) \Delta G^S \right. \tag{13}$$

Taking into account the change in chemical potentials of the solvent molecules $\Delta G^S_{\text{exch}}$, which are in smooth contact with the reactant and products, restores the concept of a true thermodynamic constant $K_{1,1,\text{exch}}^{\text{Ln(hfa)},1,3}$ expressed at infinite dilution (Fig. 13b), a procedure which should be extended for polymeric receptors in a near future for a safe discussion of allosteric cooperativity factors.

5. Conclusion and perspectives.

Except for Wolf Type III metallopolymers, \textit{i.e.} coordination polymers and/or metal organic frameworks (MOFs), which are obtained by the lucky crystallization of usually intractable mixtures of multidentate bridging ligands and metallic salts, the production of Wolf Type I and II metallopolymers is dominated by systematic, but controlled organic syntheses followed by empirical (uncontrolled) metal loading. The resulting electronic, magnetic and optical properties of these rough materials are however thoroughly investigated for their potential modulation under external stimuli. Such a pragmatic approach prevents the instructed design of metallopolymers displaying predetermined structure-function relationships. Benefiting from the achievements gained during the thermodynamic modelling of (i) self-assembled supramolecular architectures,\cite{11}-\cite{13},\cite{24},\cite{36},\cite{37} and (ii) multiple protonations of polyelectrolytes,\cite{25},\cite{26},\cite{38} the site-binding model appears to be well suited for catching the free energy changes accompanying the metal loading of soluble linear metallopolymers, thus offering unprecedented opportunities for rationalization. Applied to lanthanidopolymers, it reveals that solvation effects master intersite interaction (i.e. allosteric cooperativity), while host-guest affinities are driven by a combination of solvation and dative bond contributions. Disappointingly, the allosteric cooperativity factors exhibited by the selected
\{P3\}^{3n}[\text{Ln(hfa)}_3]_{\text{m}}\} lanthanidopolymers rarely exceed thermal energy at room temperature, which prevent specific metal organizations in these systems. The geometrical changes provided by specific disubstituted phenyl bridges in dimer D1-D3 indeed affect intersite interactions (Fig. 10b), and its magnifying to reach \(\Delta E_{\text{MM}}^{\text{MM}} > RT\) was observed with an unsymmetrical guest in \{D2[\text{Ln(pbta)}_3]_2\} (Fig. 11). These small allosteric cooperativity factors currently represent a major obstacle for attracting the interest of the broad chemical and material communities for investing more efforts in the rational design of metallopolymers. We can bet that, as soon as a safe protocol leading to a predictive clustering, or alternation of metal ions along one or more dimensions will be in hand, for instance by approaching the metallic centers, applications in the fields of directional energy migration\cite{39}, drug sensing\cite{40}, light-upconversion\cite{41} and metal segregation\cite{42} will rapidly transforms this topics into a fashionable chemical challenge.

REFERENCES AND NOTES


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All the pertinent information concerning the metal loading of linear organic polymers can be obtained from the analysis of the experimental binding isotherms (orange traces) with the help of the site-binding model. The resulting intrinsic affinities (grey arrows) and intersite interaction (blue arrow) provide a rational and instructed toolkit for programming metal organization and communication in metallopolymers.