

DNA binding with metallocomplexes of lanthanide (III) in solution

Natalia A. Komolkina¹, Marina A. Uvarova², Nina A. Kasyanenko¹

1. Faculty of Physics of Saint Petersburg State University, Saint Petersburg, Russia,
2. Kurnakov Institute of General and Inorganic Chemistry of the Russian Academy of Sciences, Moscow, Russia

n.komolkina@spbu.ru



Introduction

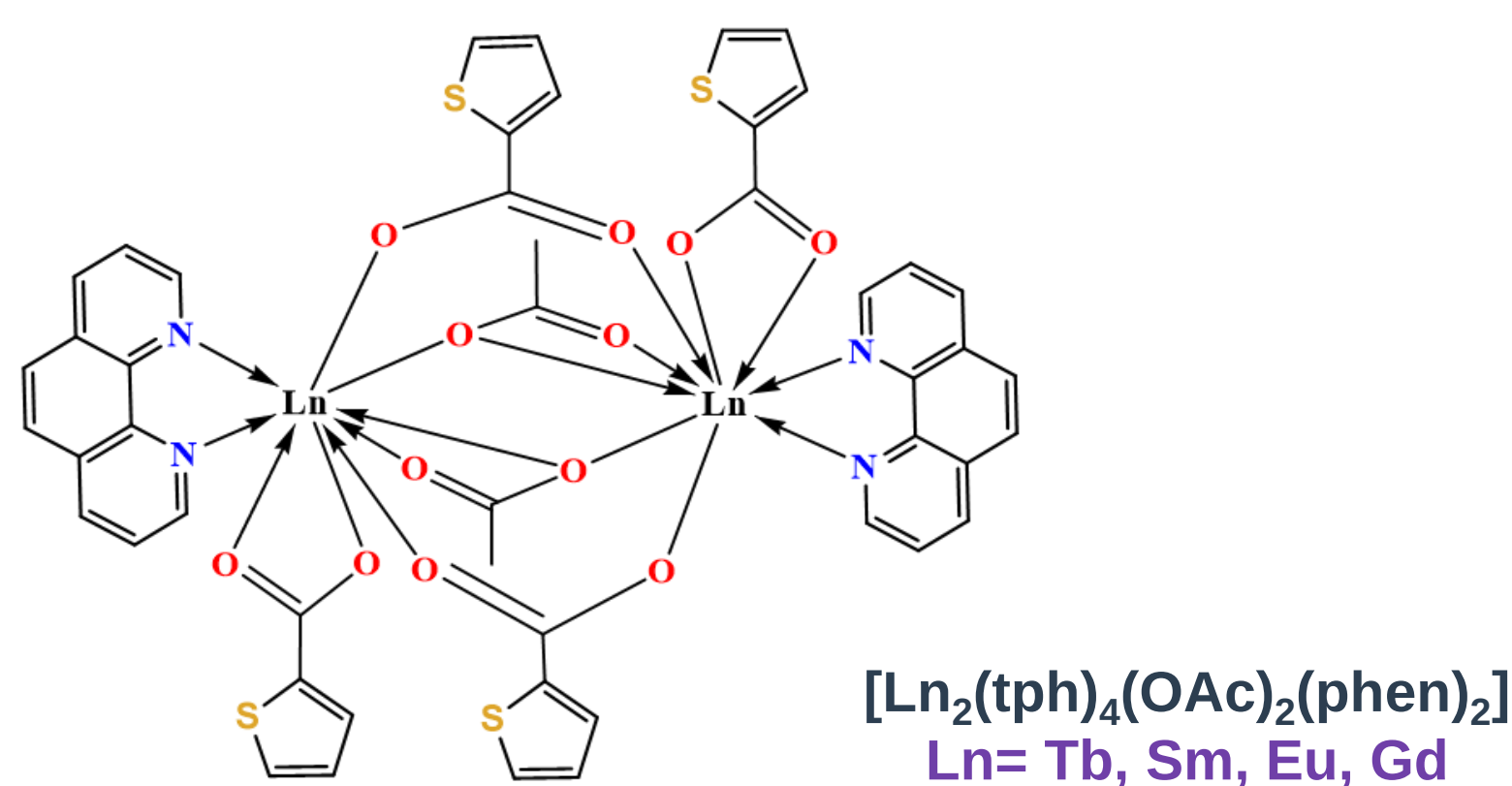
Coordination compounds of metals are actively developed as potential anticancer drugs since the discovery of cisplatin. Lanthanide (III) compounds occupy a special place among biologically active metal complexes due to their luminescence properties, as well as antibacterial and anticancer activity.

The interaction of metallocomplexes with DNA in solution is the first step of their testing since DNA is the main target for antitumor drugs of this class.

The objective of the work

To examine the interaction of four Ln(III) thiophencarboxylate complexes with DNA in aqueous solution and to propose the model of binding

Compounds and Structure



Results and Discussion

Fig.1 demonstrates an example of spectrophotometric titration of one of the compounds with Eu(III) as a metal ion. Other compounds show similar results. All investigated compounds interact with DNA in aqueous-salt solutions.

A hypochromic effect in the absorbance of Lanthanides(III) under study in complexes with DNA was observed for all compounds upon DNA titration. The calculated spectra of lanthanides were used for the analysis due to the intersection of the absorption bands of DNA and La(III) compounds. The type of changes indicates the hypochromism and the red shift of the long-waves band. The chromophores of the compounds are involved into the binding.

Fluorescent titration reveals the pronounced quenching the luminescent ion of lanthanides in solutions with DNA. The decrease in DNA solution viscosity indicates a shrinkage of the DNA molecular coil. Two types of binding is observed. First type indicates the binding to DNA of compounds via the phenanthroline ligands. The second type shows the collapse of DNA at high C(La) due to the electrostatic interactions.

DNA melting studies show that low concentration of the Ln^{III} complexes do not significantly affect the stability of the DNA double helix. Increasing concentration of compounds causes an increase in DNA melting temperature. That is, the 1st type of binding that stabilizes DNA helix.

Conclusion

The combined experimental data reveal a concentration-dependent interaction of the Ln(III) complexes with DNA, two types of binding are indicated in DNA-lanthanide complexes

Methodology

- UV-Vis spectroscopy
- Fluorescence spectroscopy
- Low-gradient viscosity
- DNA melting

Calf thymus DNA (Sigma-Aldrich) with M=18 000 base pairs was used.

The interaction of the Ln(III) complexes with DNA was investigated in an aqueous 5mM NaCl solution.

Spectra of DNA complexes with Lanthanides (III)

Uv-Vis spectroscopy

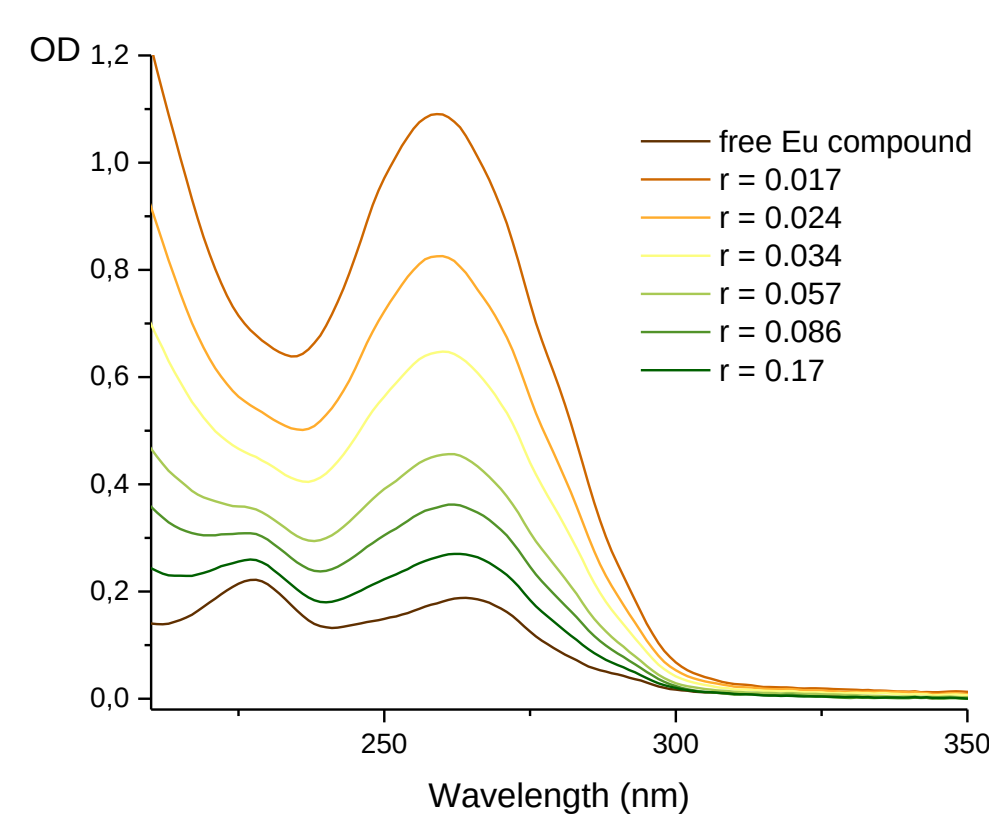


Fig. 1. Result of titration, $C(\text{Eu-complex}) = 0.13 \times 10^{-5} \text{ M} = \text{constant}$, $r = [\text{ligand}] \text{ M} / [\text{DNA}] \text{ M bp}$

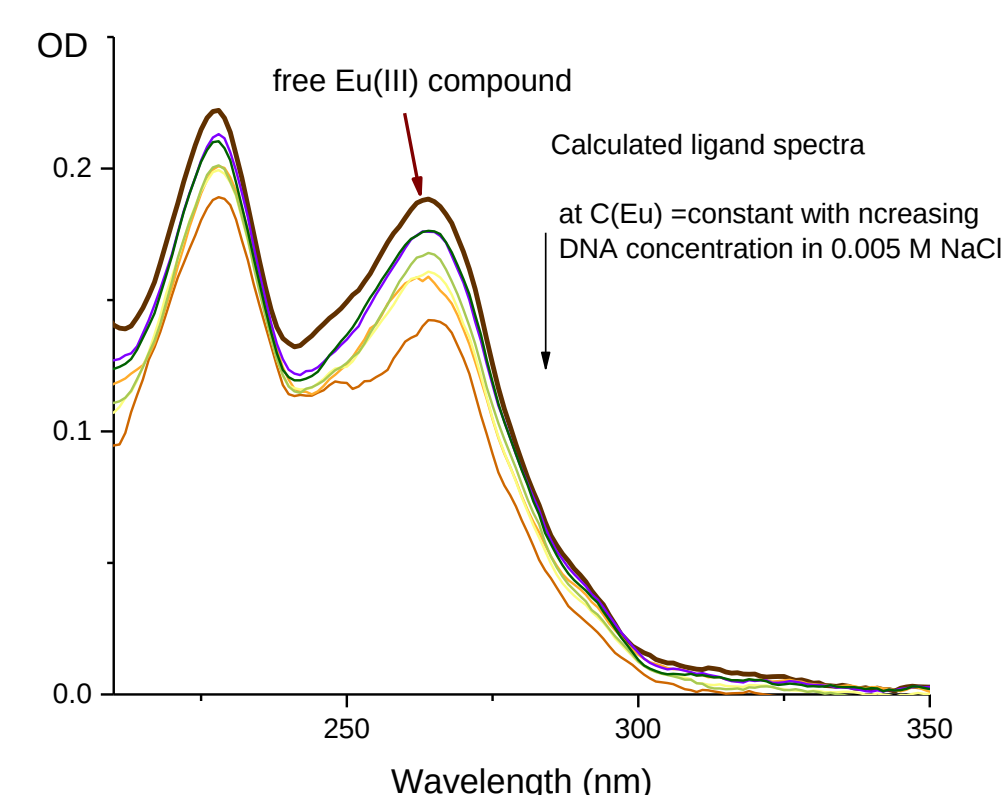


Fig.2. Calculated spectra of the Eu(III) in complexes with DNA

Fluorescence spectroscopy

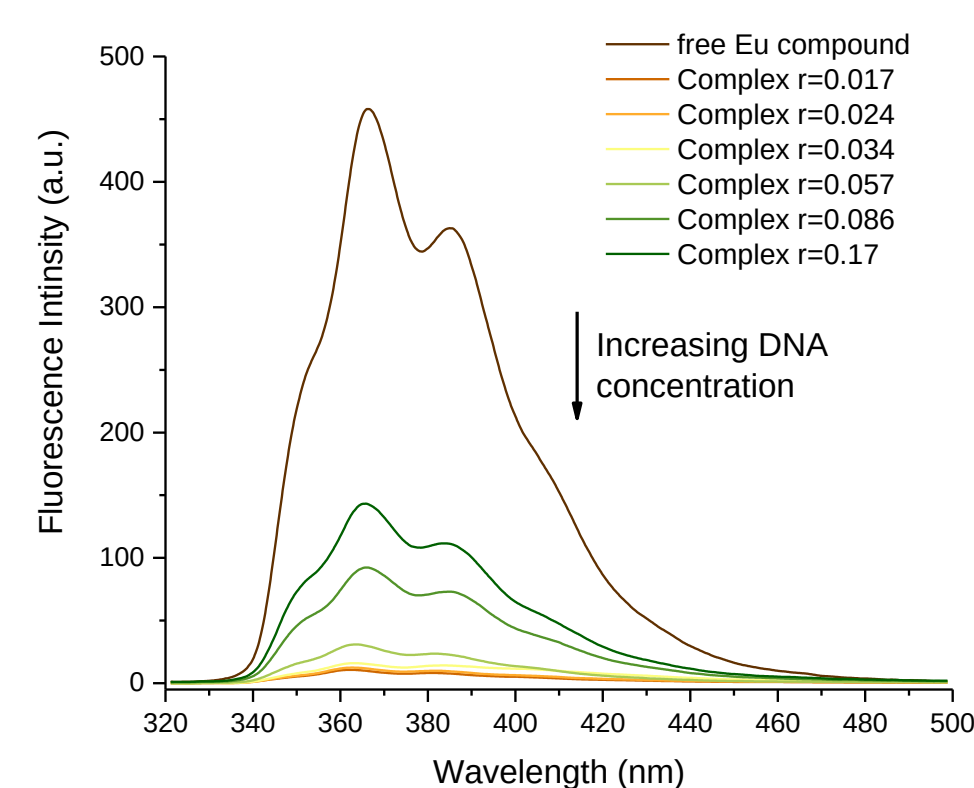
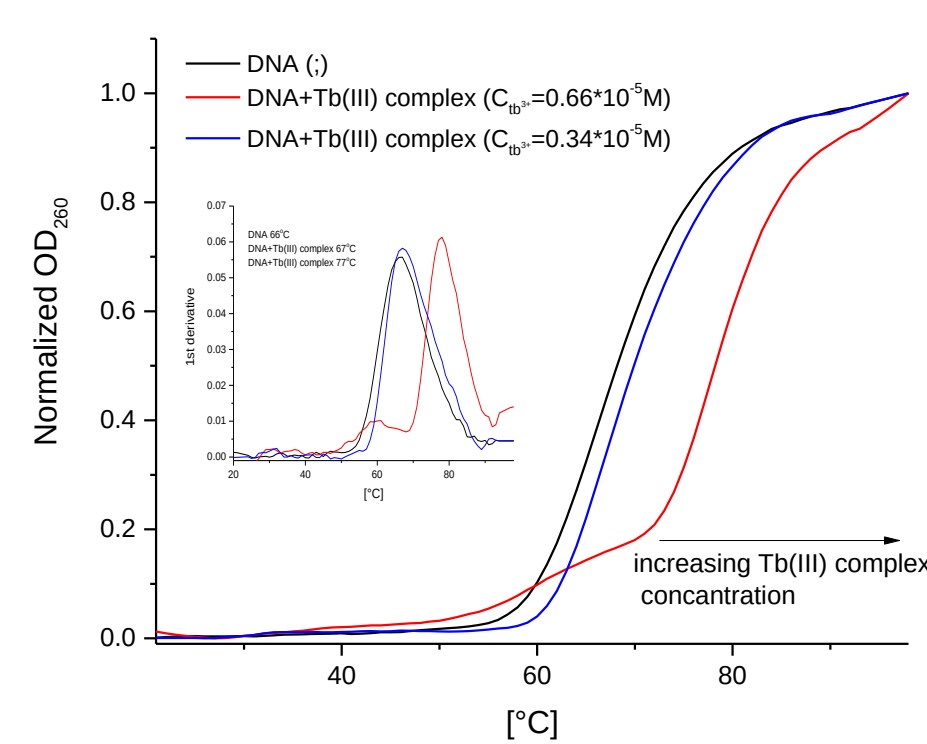
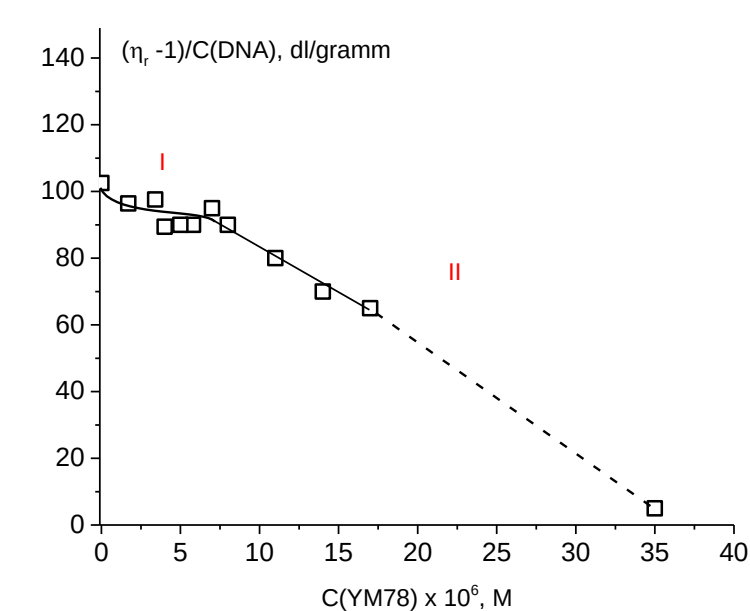


Fig.3. Titration of the Eu(III) complex with DNA

Melting assay



Low-gradient viscosity



Tb(III) complex with DNA