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Invited Feature Article

Metal complexes and time-resolved photoluminescence spectroscopy for sensing applications

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ABSTRACT

This feature article will cover our efforts to sense biologically relevant molecules using photoluminescent metal complexes. Photoluminescent metal complexes possess large Stokes shifts, long lifetimes and tunable photoluminescence maxima. We have developed probes for DNA and RNA detection containing metal complexes of ruthenium and iridium as photoluminescent reporters. Iridium complexes have also been modified to serve as probes for amino acids such as cysteine, homocysteine, and histidine. In addition, probes sensible to the aggregation state of proteins such as amyloid-β and alpha-synuclein were developed, which display changes in photoluminescence (ruthenium dipyridophenazine complexes) or birefringence (ruthenium red). Finally, we will present the detection of solvent vapors using a photoluminescent rhenium complex within a zeolite matrix. The long photoluminescence lifetime of the aforementioned complexes has been synergistically combined with advanced time-resolved methods to enhance the detection scope of these probes. For example techniques such as time-gating have been used to detect oligonucleotides, amino acids and protein aggregation even in highly autofluorescent media. Time-gating allows selecting a time-window in a time-resolved emission spectrum where the long-lived photoluminescence of the probes can be preferentially detected from the short-lived autofluorescence of the medium. In addition, we have used time-resolved photoluminescence spectroscopy to extract the photoluminescence of free histidine from the photoluminescence of histidine-containing proteins. Also, a combination of photoluminescence intensity, maximum and lifetime was used to detect solvent vapors. These examples testify on the advantages of time-resolved photoluminescence spectroscopy for enhancing the detection of analytes using probes with long-lived photoluminescence.

1. Introduction

Photoactive metal complexes have been the target of intense research in the last few decades due to their potential use in solar energy conversion schemes [1–4], bioimaging [5], and the fabrication of light emitting diodes [6]. Metal complexes with d^6 configurations such as Re(I), Ru(II) and Ir(III) can present photoluminescence emissions in different parts of the visible spectrum [2,7]. The most studied photoluminescent metal complex is tris(2,2′-bipyridine) ruthenium(II) $[Ru(bpy)_3]^{2+}$ [1,8]. We will briefly summarize the excited state properties of $[Ru(bpy)_3]^{2+}$ as a model for d^6 metal complexes. For $[Ru(bpy)_3]^{2+}$ – which has a D_3 symmetry – the metal d orbitals are split by the surrounding ligands into a low lying t_{2g} and a higher energy e_g orbitals. In a strong field configuration, such as the complexes described in this manuscript, the t_{2g} level is completely populated by 6 electrons. Direct excitation from the t_{2g} to the e_g level is forbidden by the selection rules and therefore this transition has a very low extinction coefficient. Nonetheless, excitation can occur from the t_{2g} to a ligand π^* orbital [1]. Since this transition occurs from a metal centered t_{2g} to a ligand centered π^* orbital, it is called a metal-to-ligand charge transfer (MLCT) state; this state is singlet in character and commonly labeled ^{1}MLCT. Ligand centered (LC) and metal centered (MC) transitions can be excited at higher energies but will decay almost immediately to the lowest laying MLCT state (Kasha's rule [9]). Then the ^{1}MLCT undergoes intersystem crossing to the ^{3}MLCT in a femtosecond time scale with a quantum efficiency of unity [1,2,7]. This ^{3}MLCT is actually a mixed singlet–triplet state due to spin–orbit coupling [1]. The observed photoluminescence is a result of the radiative deactivation of this mixed MLCT.

The special electronic structure that arises due to the combination of the metal cation and the coordinating ligands to form the metal complex has a profound effect in its photoluminescence. First, excitation occurs to a singlet excited state,

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which undergoes intersystem crossing to a stabilized triplet excited state. Since singlet excited states are of higher energy than their homologous triplet states, d^6 metal polypyridine complexes possess large Stokes shifts. Secondly, since the emission occurs from an excited state with a strong triplet character, the radiative transition to the singlet ground state is spin forbidden, and therefore the photoluminescence lifetime can have values from hundred of nanoseconds to microseconds. The emission spectra of these long-lived excited states can be easily resolved in time allowing to obtain time-resolved emission spectra (TRES). The advantage of TRES is that the photoluminescence spectrum can be obtained at a specific time or time-window [10]. The judicious selection of this time window allows to discriminate short-lived signals that would otherwise overlap and interfere with the photoluminescence of the metal complexes [11].

In this featured article we will present the use of metal complexes of iridium, ruthenium and rhenium for different sensing applications (Fig. 1). Iridium complexes will be used for the detection of amino acids [12,13]. Ruthenium and iridium probes will be effectively used to detect specific oligonucleotide sequences [11,14]. We will also show how ruthenium dipyridophenazine complexes can be used to monitor protein aggregation [15–17]. Finally, we will present how advanced materials containing rhenium complexes can be used for detecting solvent vapors [18]. The use of metal complexes with long-lived excited states is of importance since it has enabled us to use time-resolved photoluminescence spectroscopy to enhance the detection of analytes, even in highly autofluorescent environments.

2. Oligonucleotides

The sensitive detection of specific DNA and RNA sequences has many important current applications such as disease diagnostics [19], identifying mutations [20], monitoring transcription [21], and tracking cellular processes [22] among others [23]. We have investigated the detection of DNA and RNA using different approaches [10,11,14,24–29,30]. A popular method for detecting DNA and RNA sequences is by using molecular beacons (MBs). A molecular beacon consists of an oligonucleotide sequence with a photoluminescent dye and a quencher at opposite ends of the strand [31]. The oligonucleotide strand forming the MB has ends that are self-complementary forming a hairpin structure (loop-stem). When the hairpin structure is formed, the dye and the quencher are close to one another and any excitation of the dye is instantaneously deactivated by the quencher without fluorescence emission (Fig. 2a, red arrow and red curve). On the other hand, addition of DNA complementary to the loop portion of the MB produces a conformational change due to the formation of double-stranded DNA, which will position the dye and the quencher at different ends of the strand [31]. The imposed distance due to the hybridization process prevents the deactivation of the dye's photoluminescence by the quencher, resulting in an increase in the emission intensity (Fig. 2a, blue arrow and blue curve).

While MBs containing organic fluorophores have been very well studied and characterized [32], MBs with inorganic metal complexes are less common [23]. Probes containing metal complexes with large Stokes shift and long lifetimes represent good additions to the toolbox for the detection of DNA and RNA. We assembled hybrid inorganic–organic MBs containing a photoluminescent metal complex and an organic quencher (Fig. 1, first column) [11]. The metal complexes used were either ruthenium(II) polypyridyl complexes or iridium(III) phenylpyridine complexes, while the organic quenchers were BHQ2 and Cy5. The employment of metal complexes with long-lived photoluminescence allows for the use of time-resolved photoluminescence spectroscopy to improve the performance of the probe. Fig. 2a shows an MB bearing an iridium complex and a BHQ2 quencher. In solution the MB has minimal photoluminescence (red curve), but upon addition of target DNA (blue curve) the emission increases up to 8 times. The conservative increase in photoluminescence is due to the relatively

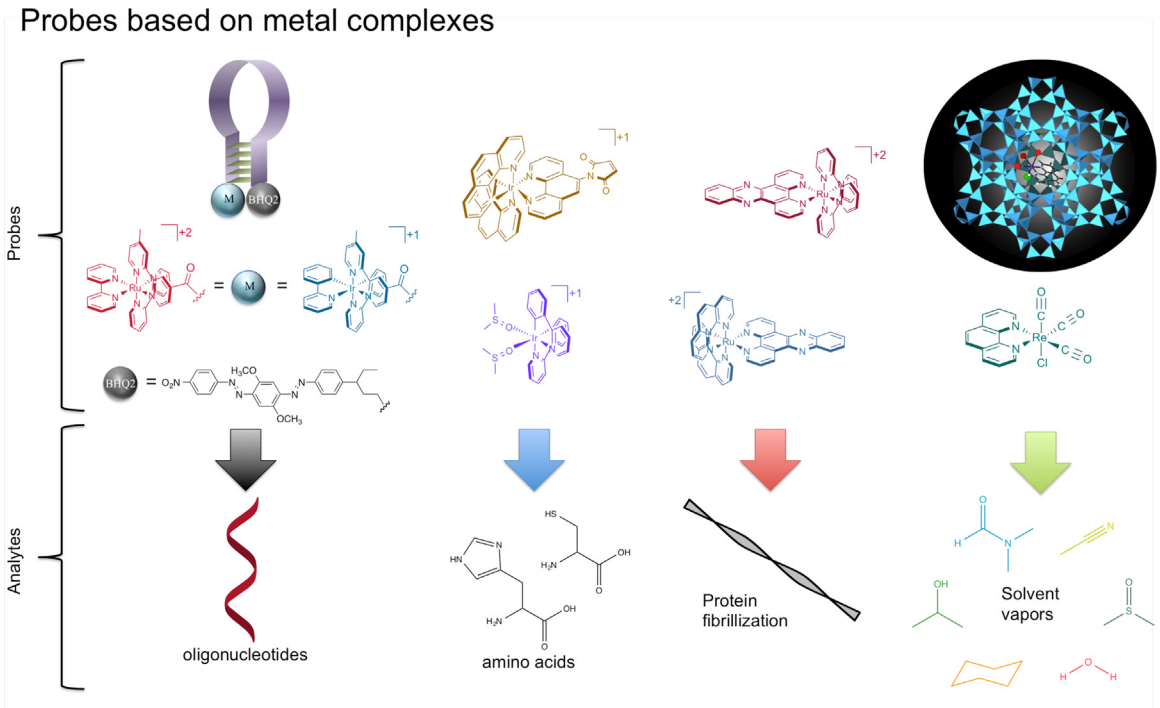

Fig. 1. Visual summary of the different probes described in this featured article. From left to right: first column, molecular beacons with iridium and ruthenium complexes for the detection of oligonucleotides; second column, iridium complexes for the detection of amino acids; third column, ruthenium dipyridophenazine complexes for sensing protein aggregation; fourth column, rhenium complex for the detection of solvent vapors.