Luminescent d^6 metal complexes for biomarker detection

Daniel Hofmann Literature Seminar October 4, 2016

Octahedral d^6 complexes have been studied in great detail for their luminescent properties. Ru^{2+}, Os^{2+}, Ir^{3+}, and Rh^{3+} have all been tested for their applications in photo-catalysis and photo-electrochemistry. d^6 metal complexes are ideal for these applications because of long phosphorescent lifetimes and high luminescence efficiencies. Many of the complexes involve a cyclometalated ligand structure. This gives rise to a mixture of ligand-to-metal charge transfer (MLCT) and $^3(\pi\text{-}\pi^*)$ ligand excited states. The 4d and 5d metal ion allow intersystem crossing from the singlet excited state to the triplet excited state due to spin-orbit coupling. The luminescence properties of d^6 metal complexes have led to research into their use in the field of biomarker detection.[1,2]

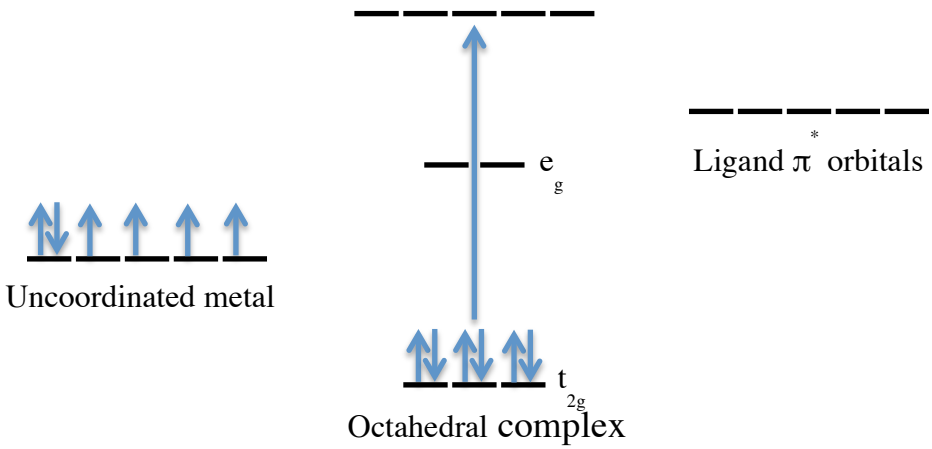

Figure 1: Metal-to-ligand charge transfer of a octahedral d^6 metal complex.

Progression of disease can be indicated by physical parameters in the body. Parameters, known as biomarkers, can be proteins, metabolites, DNA, lipids, mRNA and other types of overexpressed signals. Some typical detection methods for biomarkers include enzyme-linked immunosorbent assay (ELISA), polymerase chain reaction (PCR), and Western blotting. These techniques can be time consuming and have tedious sample preparation. Metal complexes can be used to detect biomarkers through a variety of luminescent techniques including switch-on/off sensing and electrochemiluminescence. Metal complexes have the benefit over enzyme based sensing because they can withstand greater changes in pH and temperature. There are also many cases where metal complexes are used in conjunction with antibodies and aptamers to increase the sensitivity and selectivity for the biomarker. Organic fluorophores are another area of research in alternatives to current sensing techniques. Metal complexes tend to have longer phosphorescent lifetimes than organic fluorophores. This allows for easier detection of the signal from the background fluorescence using time-resolved fluorescent spectroscopy. The larger stokes shift of metal complexes helps to avoid self-quenching. The modular synthesis of metal

complexes allows their structure to be modified easily and therefore luminescent properties can be tuned. [1-3]

Iridium (III) complexes are promising in the field of luminescent biomarker detection. Iridium (III) complexes have an advantage over ruthenium (II) complexes in their higher quantum efficiencies for color tuning due to limited ligand-field splitting energies of the ruthenium ions in their complexes. Cyclometalated Ir (III) complexes have been shown to exhibit this color tunability better than other structures.[1,2,3] The Ma group has synthesized Ir (III) complexes that are selective for the G-quadraplex structure. An assay was established using this complex for the detection of protein tyrosine kinase-7 (PTK7). PTK7 is a cell membrane protein that is a biomarker for a range of leukemias and solid tumors. The experimental layout features an aptamer sequence, selective for PTK7, that is attached to a guanine-rich sequence.[4] The aptamer sequence is determined using the systematic evolution of ligands by exponential enrichment (SELEX).[5] The addition of PTK7 coordinates the aptamer sequence to PTK7. The G-quadraplex structure is formed with the addition of potassium ion and the G-quadraplex structure is coordinated to the Ir (III) complex for the luminescent signal. [4]

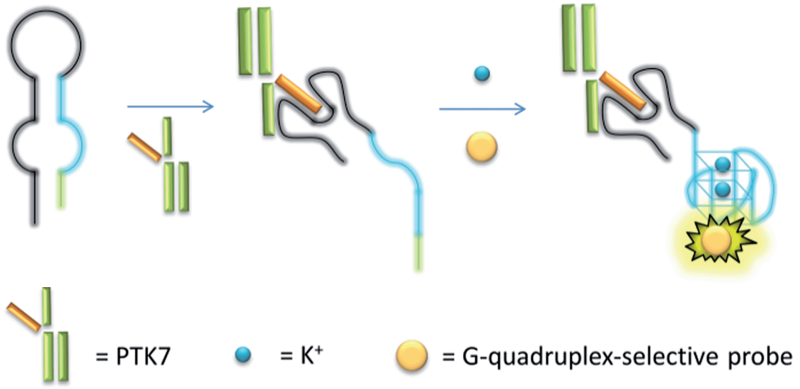

Figure 2: Experimental set-up for the detection of PTK7 where the black line is the PTK7 aptamer binding sequence and the blue and green line are the guanine-rich G-quadraplex forming sequence.

Electrochemiluminescence is a process where an intermediate is electrochemically produced and then undergoes an exergonic reaction to produce an excited state. This excited state will then emit light as it relaxes to its ground state.[6] A electrochemiluminescent immunosensor using a Ru (II) complexes has been developed by Xiao et al for the detection of the cancer biomarker, α-fetoprotein (AFP). This detection method was developed by combing a Ru (II) complex, 3,4,9,10-perylenetetracarboxylic acid (PTCA), and graphene to form a nanocomposite structure. This system has high sensitivity for tripropylamine (TPA) as a coreactant. For the detection of AFP, chitosan and the nanocomposite are placed on a glassy carbon electrode. The amino groups of the chitosan link to anti-AFP by gluteraldehyde. The immunoreaction of AFP in the presence of anti-AFP will hinder the diffusion of TPA to the electrode and there will be a decreased ECL signal. [7]

The luminescence of the $Ru(bpy)_3^{2+}$ was first documented in 1959 by Paris and Brandt.[8] The system has been studied extensively in the years since. The $Ru(bpy)_3^{2+}$ has been very successful in the field of electrochemiluminescence for its efficiency and sensitivity.[9,10] Wang et al have developed a derivative of the $Ru(bpy)_3^{2+}$ with a bis(2,2′-bipyridyl)(4′-methyl-[2,2′]-bipyridinyl-4-carboxylicacid) ruthenium(II) with the coreactant tris(3-aminopropyl)amine (TAPA). These compounds were used as precursors to form nanorods that, with the aid of an antibody sandwich structure, can detect N-acetyl-β-D-glucosaminidase (NAG), a biomarker for diabetic nephroparthy (DN). [11]

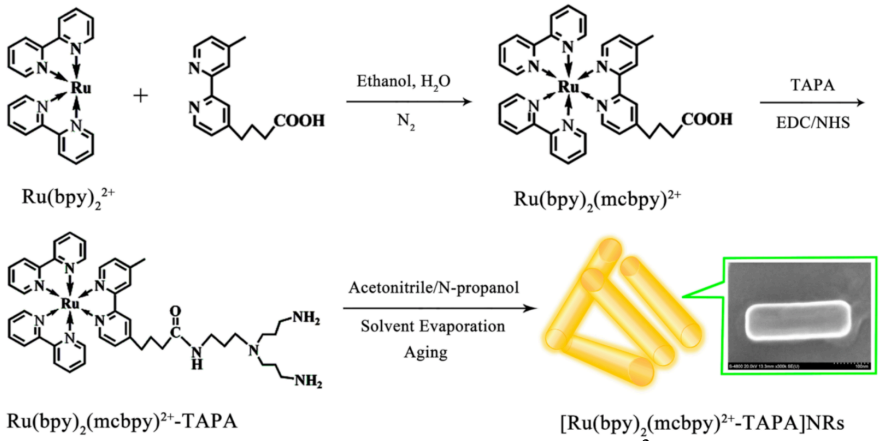

Figure 3: Schematic for the synthesis of $Ru(bpy)_2(mcbpy)^{2+}$ -TAPA nanorods.

Biomarker detection using metal complexes is a promising field. Some metal complex assays may suffer slightly in detection limits compared to current sensing techniques like ELISA but many assays are on par with current techniques. Metal complexes also have the rugged advantage that they can be potentially used in developing countries where certain diseases are prominent and the technology is not present for current sensing on site. The increasing selectivity and sensitivity that is being exhibited by using aptamers/antibodies and increased efficiency with nanomaterial techniques has the potential to drive these metal complexes into contention with ELISA and other current sensing techniques.

References

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