METAL COMPLEXES AS PROBES

PROF. R. CHANDRA
Professor
Department of Chemistry

INTRODUCTION

- Metal complexes are the best tools to probes the biological system
- Metal complex can teach us the biology of living cells
- The properties which make them suitable for biological probes are:

  - Ability to bind with biological moieties
  - Metal complex can form chelate
  - Metal complex can be cationic, anionic and neutral
  - Different interactions with ligands
  - Metal complex can have photophysical properties
  - Transition metal complex have partially filled d shell which impart magnetic and electrical properties to complex

Metal complex for probing DNA

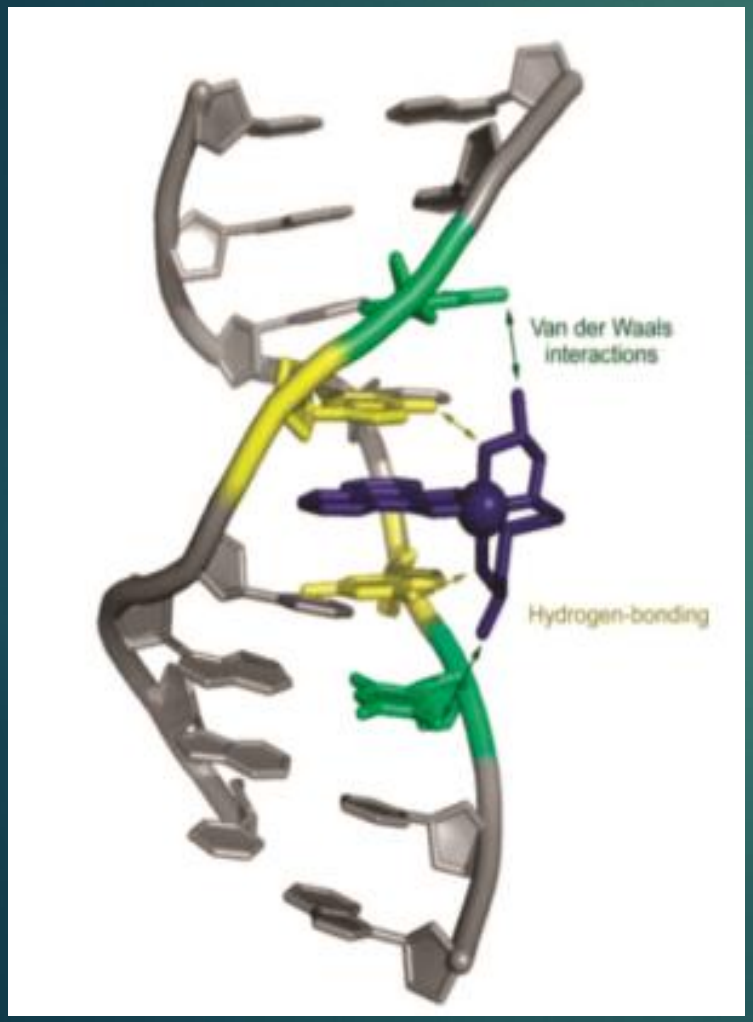
- Metal complex are well suited for DNA interaction because of the positively charged metal center can attracted towards the negatively charged phosphate back bone of DNA
- Metal complex can fit into base stacks and groove of targeted DNA sequences
- Metal complex must have three dimensional structure and rigidity

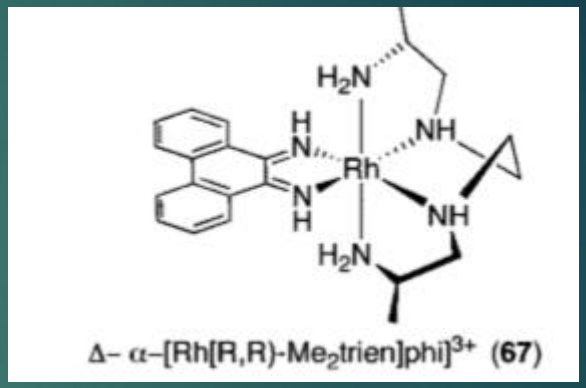
- Metal complex should be fluxional in behavior to negate selectivity based on shape recognition
- Stereochemistry of complex can provide an element of enantioselectivity because DNA its self is chiral
- The complex with photophysical properties serve as DNA foot printing agents

Sequence specific DNA probes

- Octahedral intercalating complexes are specific for DNA sequences
- Intercalation is a DNA binding mode in which a planar aromatic group inserts and ∏-stacks between two adjacent base in the core of a DNA double helix
- For this metal complex must contain at lest one large planar aromatic ligand
- This is the non covalent interaction and give solvatochromic luminescence

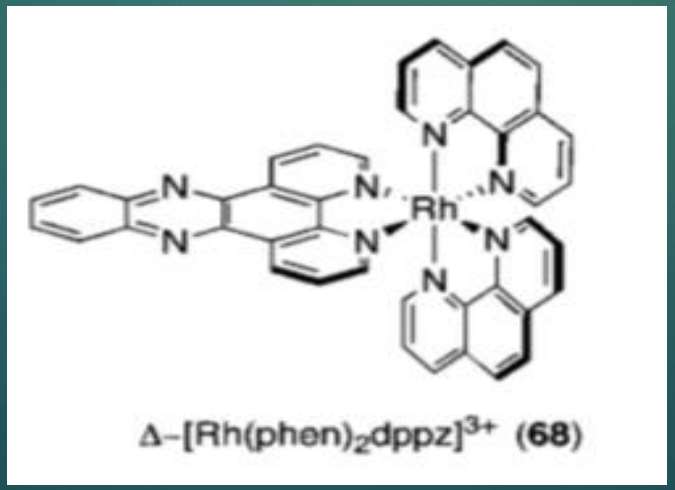
Intercalation of complex





rhodium complex bound with 5-TGCA-3 sequence of DNA.

- The complex given below, in aqueous solution hydrogen bonding with N of dppz deactivates the excited state and quenches the fluorescence.
- When DNA is added to the solution the complex shows its characteristic luminescence by intercalation into the base stacks, shielding hydrogen bonding with dppz ligand.



Δ–[Rh(phen)$_2$dppz]$^{3+}$ (68)

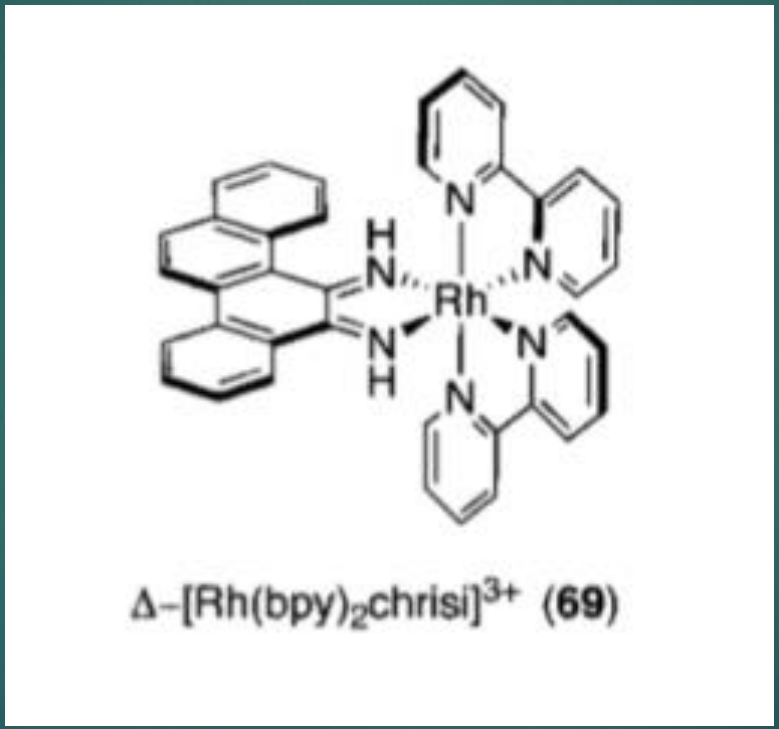
Metal complex that recognize mismatched DNA

- Mismatched base pair are result of error in DNA replication.
- mismatched base pair leads to genetic mutation.
- Mismatched base pair may cause cancers and solid tumors
- Metal complex using the expensive 5,6-chrissene quinone ligand like $[Rh(bpy)(chrisi)_2]^{3+}$ can bind with mismatched base pair atleast 1000 times stronger than the matched base pair.

- Mismatched Selective complex use a planar aromatic ligand that is too wide to fit into a normal DNA groove

- The larger DNA ligand can not intercalate the into normal matched DNA but in case of mismatched DNA the duplex is thermodynamically destabilized their destabilization allows the large ligand to eject the mismatched base pair and replace with its own inserting ligand.

A Rhodium complex given below attached to a cell penetrating polyarginine peptide and fluorophore was tested in the cells and shown to localise in the nucleus

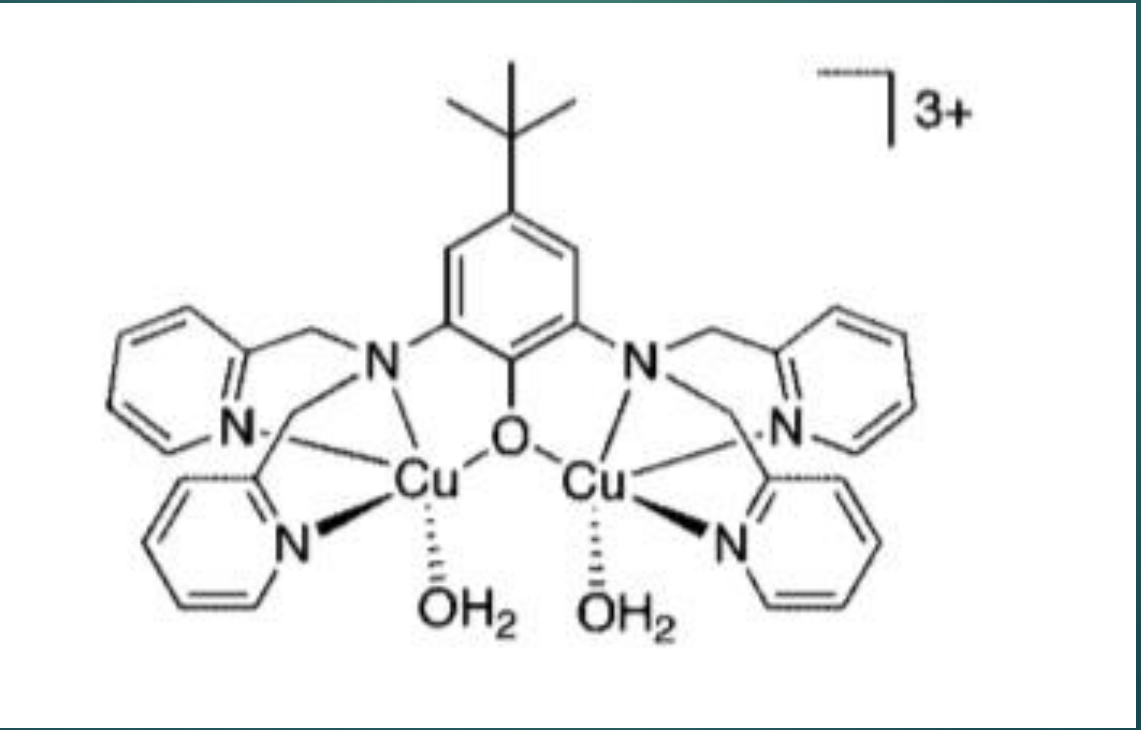


Δ–[Rh(bpy)$_2$chrisi]$^{3+}$ (**69**)

Metal complex that recognized single-double strand junctions

- A class of binuclear and trinuclear copper complexes has demonstrated exquisite selectivity in oxidizing DNA at ss/ds DNA junctions
- Complex of binuclear copper are also sequence selective, and preferring to oxidized guanine at n and n+1 position of ss DNA directly extended from duplex region
- ss/ds targeting complex have not been fully developed.

Binuclear copper complex that recognise ss/ds junctions



Luminescent transition metal complex as probes

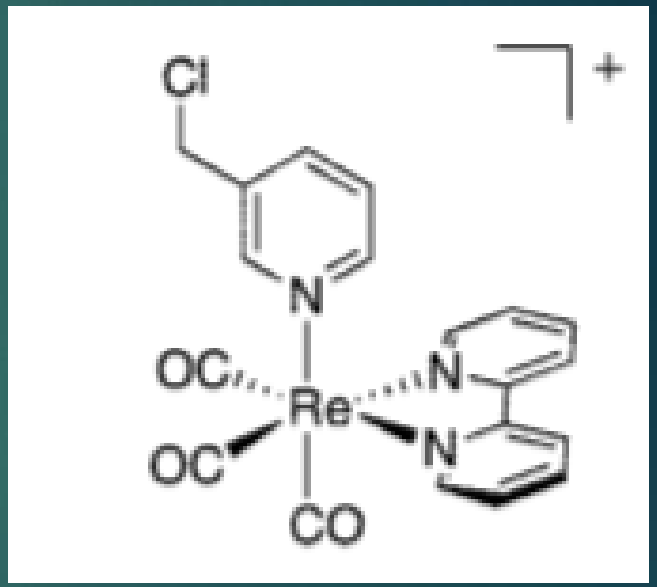
- These complex are specifically designed to target DNA

Example: Rhenium tricarbonyl useful in vivo probes . The luminescence stems from a metal to ligand charge transfer triplet excited state

- The complex have large stokes shift (187nm) long fluorescence life time and good quantum yield.

Luminescent metal complex as probes

- The tricarbonyl Rhenium(I) cation in human MCF-cells this membrane permeable dye localizes to the mitochondria.



- The selective localization is due to the reaction of chloromethyl group with thiols that are concentrated in mitochondria.

METAL COMPLEX AS MRI CONTRASTING AGENT

- MRI Provide 3D image of opaque biological structure with high resolution.
- MR images derives from the nuclear magnetic resonance of water proton,
- The contrast in the image depends on the local concentration of water and the relaxation time of proton which can be significantly reduced if the spin are in the contact of local paramagnetic center thereby brightening the image

example : $[Gd(DTPA)(H_2O)]^{2-}$.

Conclusion

- The application of metal chelating agents, coordination complex, and organometallic complex in cell biology offers diverse opportunities for manipulating biological processes.

- Application of inorganic complexes is exciting and also present ongoing challenges these kind of reagents become more frequently used in biological studies.