

# A Review of Bis-Porphyrin Nucleoside Spacers for Molecular Recognition

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**Abstract:** These spacers can create tailor-made recognition motifs that recognize specific molecules or molecular structures. The bis-porphyrin nucleoside spacers allow for greater flexibility and accuracy in the design of recognition motifs, leading to improved molecular recognition. This makes it possible to create custom recognition motifs for various applications, such as drug target identification and drug delivery. Bis-porphyrin nucleoside spacers can also build complicated recognition motifs with many recognition sites. This allows the creation of highly precise recognition motifs for many targets, improving medication delivery and efficacy. This can drastically cut drug dosage, lowering adverse effects and expense. High stability makes recognition motifs appropriate for long-term applications. Several disorders have been treated with encouraging outcomes using this technology. It could change medicine delivery and improve focused treatments. This technology will grow more significant as more applications are developed to serve more people. It could transform the healthcare business and improve disease treatment. It could save time and money by simplifying therapies and increasing patient outcomes. It can also lower treatment costs and make them more accessible. It can also help doctors make better judgments and deliver better care by providing more accurate and timely patient insights. More dependable and accurate than traditional treatments, AI-driven medical treatments reduce errors and patient harm. Doctors and healthcare providers are increasingly using AI-driven medicinal treatments. AI-driven medical treatments are cheaper than traditional ones, saving healthcare providers money. AI-driven treatments can also speed up diagnosis and treatment, saving time and money.

**Keywords:** Light-Harvesting; Reaction Center; Antenna Effect; Electron Transfer; Dexter Type; Förster Type; Doctors and Healthcare; AI-Driven Medical Treatments.

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## 1. Introduction

### 1.1. General information on photosynthesis

Photosynthesis is a biochemical process that converts the energy [1]-[3] of light into the chemical energy that allows the production of sugars. This is a fairly complex process found in plants and some bacteria. Photosynthesis occurs in the chloroplasts of plant cells or specialized regions of the cell membrane of prokaryotic cells [1]. It is a process that requires light, carbon dioxide, and water to produce glucose and oxygen. The oxygen produced is released into the atmosphere, while the plant uses glucose for energy [2]. Photosynthesis is an essential process for the survival of plants and other organisms. It is also important for the global carbon cycle, as it helps to remove carbon dioxide from the atmosphere. This process is also essential for sustaining life on Earth, as it produces the oxygen that all living things need to survive. It also helps regulate the global

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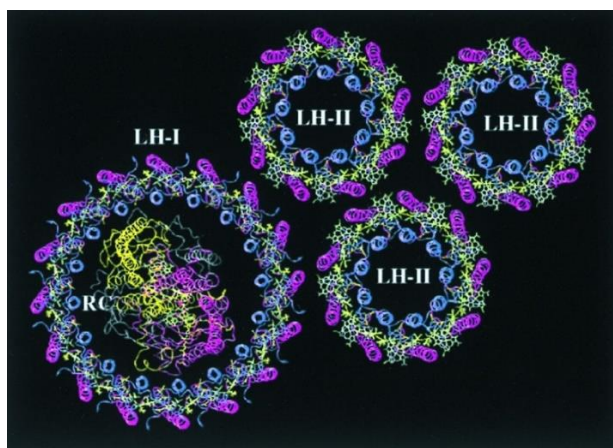
climate by sequestering carbon dioxide from the atmosphere. Photosynthesis also produces carbohydrates, essential for plant growth and development and provides energy for animals that consume them [4]-[6].

Light energy is converted into chemical energy, which produces carbohydrates like glucose. Visible light has wavelengths ranging from blue (200nm) to red (850nm), and ultraviolet light (about 300nm) has more energy but is mostly absorbed by our atmosphere. The ozone layer helps to protect us from the dangerous ultraviolet light. The most significant step in photosynthesis is when charges are separated through transmembrane complexes of protein-pigment types known as reaction centres. In 1984, Deisenhofer et al. [5] successfully crystallised and resolved the atomic structure of a transmembrane protein from a photosynthetic purple bacterium. This work won the Nobel Prize in 1988. Investigating photosynthetic bacteria is beneficial for understanding the reaction centres, and chlorophyll pigments collect light from collecting antennas before it is transferred to the reaction centres. This, in turn, helps researchers understand how energy is converted and stored in the form of chemical energy, which can then be used for metabolic processes. Such studies are essential to furthering our understanding of photosynthesis and its applications in biotechnology. Understanding photosynthesis in bacteria can also provide insight into the evolution of photosynthesis and energy metabolism in plants and other photosynthetic organisms. It can help us understand the origin and evolution of life on Earth and its future potential [6]-[8].

## 2. Light Energy Collecting Antennas

### 2.1. Description of the collector antennas

Once the photosynthetic apparatus was studied, the mechanisms of photosynthesis could be comprehended further. McDermott et al. revealed the atomic structure of the light-harvesting bacterial complex LH2. This discovery is an integral step in finishing the structure of the RC founded by Deisenhofer et al. [6]. All photosynthetic organisms have chlorophyll pigments that comprise photonic collecting antennas, typically located inside the photosynthetic membrane near the CR. These pigments, which can be carotenoids and chlorophylls, can absorb light from various spectrums. Most photosynthetic bacteria have at least two polypeptide complexes with biochemical or spectroscopic properties. Photonic energy will pass through a few complexes or light collectors (LH). The LH2 complex is the outdoor antenna responsible for capturing light energy and sending it to the LH1 indoor antenna close to the CR. The structure of the indoor antenna, LH1, was determined by X-ray crystallography [9]-[11]. The resolution of the LH1 complex shows that this complex is made from the same type of molecular units as the LH2 complex. However, the LH1 complex is much bigger since it hosts the CR. The LH1 complex consists of the Light-Harvesting 1 and the Charge Retention. The Light-Harvesting 1 captures the light energy and transfers it to the Charge Retention. The Charge Retention is responsible for storing the energy until it is needed. The LH1 complex is essential for the functioning of photosynthetic bacteria as it is responsible for capturing and storing light energy. Without it, photosynthesis would not be possible. The photosynthetic bacteria then use this energy to produce the energy-rich molecules essential for their growth and survival. The LH1 complex is a key component of the photosynthetic process, and without it, many organisms would not be able to survive.



**Figure 1:** Diagram of the LH2 and LH1 complexes harvesting light energy before transferring it to the reaction centre (CR) [8]

### 2.2. Schematic description of the process of collecting light energy

The light-capturing protein complexes LH1 and LH2 form an antenna shape that can maximize the use of the small amount of light available. When one of the larger LH1 complexes is exposed to light, the energy is passed between them until it reaches a free reaction centre. The researchers observed that if an LH1 complex captures light while its reaction center is busy, it will

pass the energy to other LH1 complexes until a reaction center is available. These LH1 complexes are a highly efficient way of capturing and transferring light energy to the reaction center. This allows them to use the small amount of light most efficiently. This energy transfer process is also known as energy funneling, which is essential for photosynthesis in low-light environments. As a result, LH1 complexes are crucial for photosynthetic organisms to survive in their environment. The LH1 complexes are, therefore, an important factor in the success of photosynthetic organisms in their environment. They are essential for the process of photosynthesis to take place in low-light environments. Without the LH1 complexes, photosynthesis would be impossible in low-light environments, resulting in the death of the photosynthetic organism. Therefore, these complexes are essential for the survival of photosynthetic organisms Figure 1.

### 2.3. Antenna effect

The composition of chlorophyll pigments and their arrangement in the photonic energy collectors LH1 and LH2 play an important role in photosynthesis. These pigments absorb a wide range of photonic energy, which is then transferred to the Reaction Center. This transfer is known as the antenna effect. Additionally, the pigments' spatial orientation helps ensure an efficient and speedy process. Finally, the light energy is converted into chemical energy at the heart of the cell membrane via a series of electron transfer reactions. This chemical energy is then used to power the cell and is eventually stored as ATP molecules. This process of energy conversion is known as photosynthesis. ATP molecules power the cell's metabolic processes, allowing it to perform its functions. This process is essential for a cell's survival and growth. This energy conversion process provides the cell with the energy it needs to sustain life and is essential for the survival of all organisms. Photosynthesis is one of the most important biochemical reactions in living organisms. Without photosynthesis, life on Earth would not be possible. It is responsible for the production of the oxygen that we breathe and the food we eat. It is the basis of all life on the planet. Photosynthesis is responsible for capturing solar energy and its conversion into chemical energy. This process is essential for the ecosystems on the planet, as it maintains the levels of oxygen and carbon dioxide in the atmosphere [4].

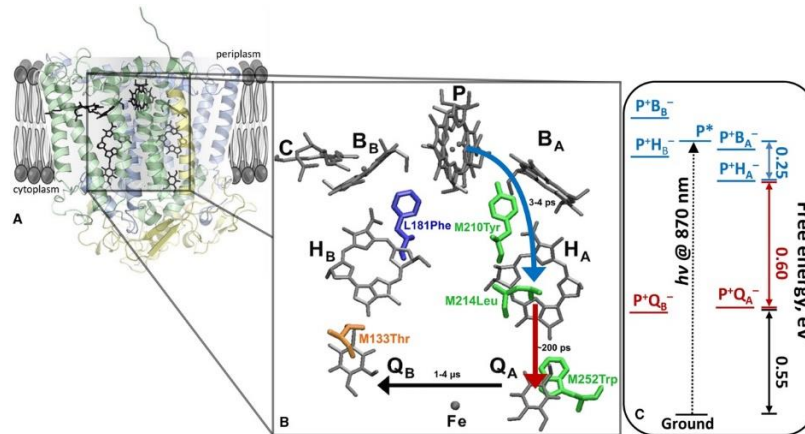
## 3. The Reaction Center, CR

### 3.1. Structure of the CR of the bacterium *Rhodospseudomonas viridis*

The photosynthetic purple bacterium *Rhodospseudomonas viridis*'s CR [8] is represented in Figure 2. [3] This CR comprises four protein parts labelled by their molecular weight. The proteins are named H (Heavy), M (Medium), L (Light) and cytochrome C [5]. These proteins are arranged in a specific order, with the H and M proteins forming the core of the CR complex. The L and cytochrome C proteins are located at the outer edges. The arrangement of the proteins is essential for the efficient functioning of the CR [8]. The four proteins are held together by weak non-covalent interactions such as electrostatic, hydrophobic, and van der Waals forces. These interactions are essential for the proper functioning of the complex. These interactions are delicate and can be easily disrupted by changes in temperature, pH, or the presence of certain chemicals. This can lead to a breakdown in the structure of the complex, resulting in a decrease in its efficiency [6]. The protein subunits M and L form the core of the complex. They consist of:

- a bacteriochlorophyll dimer (BCp) called a special pair (P)
- two accessory bacteriochlorophylls (BCA)
- two bacteriophytins (BP)
- of a non-heme iron atom probably having a structural role
- two quinones, menaquinone Q A and ubiquinone QB

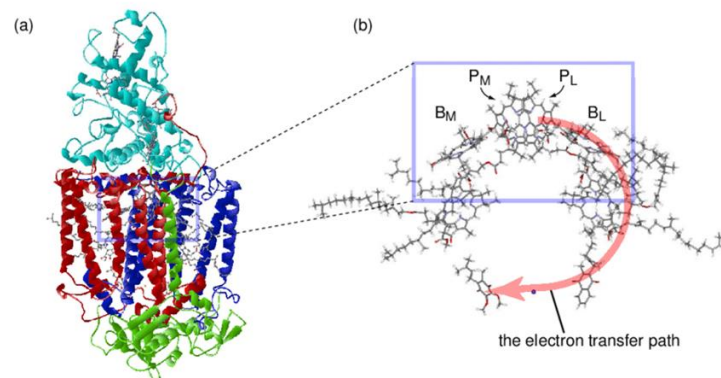
The special pair of P absorb light energy and act as electron donors, while the BP of the L protein and the two quinones take the role of electron acceptors<sup>7</sup>. The exact role of BCA is still unknown. Cytochrome C has four hemic groups connecting with the L and M subunits on the periplasmic surface. Most of the H protein interacts with the L and M proteins on the cytoplasmic side, and its total length is 130 Å. The H protein is believed to be involved in electron transfer from the P protein to the quinones. It is also thought to have a role in the assembly of the cytochrome bc<sub>1</sub> complex. The exact role of BCA is still unknown, but research suggests that it plays a critical role in the electron transport chain. Its structure and function are being studied to gain further insights into its role. BCA is believed to be essential for energy production in the cell, as it transfers electrons from the respiratory chain to the quinones. Its importance is further demonstrated by its presence in all known organisms, from bacteria to humans. BCA has been identified as a source of reactive oxygen species, which can cause oxidative stress in cells. This suggests that BCA may also be involved in regulating cellular metabolism. Further research is needed to understand the exact role of BCA in the electron transport chain and its effects on cell physiology. BCA's role in energy production and maintenance of cellular homeostasis is evident. Therefore, exploring the implications of BCA in health and disease and its potential use as a therapeutic target is important. BCA's potential to modulate energy metabolism and cellular homeostasis is an area of interest that warrants further investigation. Such research could lead to novel insights into regulating mitochondrial function in health and disease.



**Figure 2:** Reaction Center of the bacterium *Rhodospseudomonas viridis* [3]

### 3.2. Photoinduced separation of loads in the CR

Chlorophyll pigments absorb light energy, which is then rapidly transferred to the reaction centre (CR). This energy causes the pigment (P) to enter an excited state, facilitating the transfer of an electron to bacteriochlorophyll along the L protein (BPL) in 3 picoseconds. The electron then migrates in 200 picoseconds to the menaquinone QA, and this reduction of QA provides the driving force for the electron transfer. This electron transfer then initiates a series of electron transfers that ultimately produce ATP and NADPH. These molecules then power the light-dependent reactions of photosynthesis. The ATP and NADPH molecules are then used as energy sources in the light-independent reactions of photosynthesis (Figure 2) [10]-[13]. This process then produces the sugar molecules that are necessary for plant growth. These sugar molecules are then used as energy sources for the plant and can also be used to create other molecules, such as proteins and fats, necessary for the plant's growth and development. The molecules created by photosynthesis can also be used as a food source for other organisms, helping to support life on Earth. Photosynthesis is thus essential for the survival of all living things on Earth, as it is the primary energy source for all organisms. It is also a key factor in global climate regulation, as it helps to absorb carbon dioxide from the atmosphere. Photosynthesis also produces oxygen, which is essential for all life on Earth. It is the basis of the food chain and is thus a critical component of the global ecosystem. Without photosynthesis, the world would be drastically different. Plants would not be able to produce food, and all living organisms would be unable to survive (Figure 3) [8].

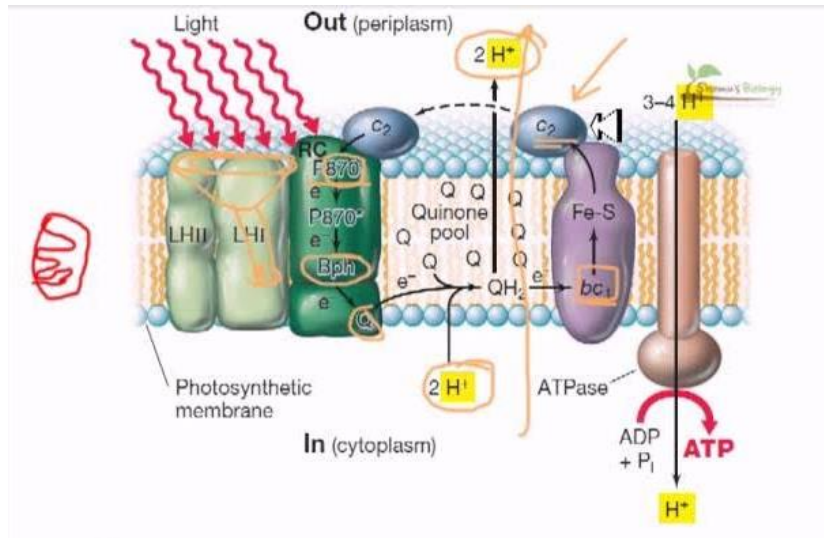


**Figure 3:** Schematic representation of the CR components of the photosynthetic bacterium *Rhodospseudomonas viridis* [11]

In the photosynthesis process, P is oxidized, and QA is reduced. The light energy is then converted into a potential difference of 590 mV. In 270 nanoseconds, P is reduced by cytochrome, and in 6 microseconds, QA is oxidized by QB. This creates a separation of charges, with the positive charge on P migrating to the cytochrome and the negative charge represented by the electron migrating in the opposite direction to QB. As a result, the electron allows photosynthesis to continue and generate ATP, which is used as a cell energy source. The overall reaction ultimately produces oxygen molecules released into the atmosphere. This oxygen is essential for the survival of many organisms, including humans. Therefore, photosynthesis is an important process that helps sustain life on Earth. This process of photosynthesis can be described as a light-dependent reaction, as it requires light energy to occur. Without photosynthesis, life on Earth as we know it would not exist. Photosynthesis is an

essential process that helps maintain the balance of oxygen and carbon dioxide in the atmosphere, which is necessary to sustain life on Earth.

### 3.3. Biological phenomena induced by this electron transfer



**Figure 4:** Diagram of the cell membrane of a photosynthetic bacterium [4,13]

When a photon interacts with the CR, it triggers an electron transfer from P to ubiquinone QB. This reduction of QB causes it to take two protons from the cytoplasm. Hydroquinone is then released into the periplasm and is oxidized, releasing two protons into the periplasm and two electrons into the CR. The cycle is then repeated with the regenerated ubiquinone QB returning to the CR. This process creates a proton gradient across the membrane that can be used to generate ATP. The proton gradient across the membrane results from the electron transfer from the photon to the CR and is used to generate ATP, providing energy to the cell. This process is known as photophosphorylation and is the basis for photosynthesis in all photosynthetic organisms. The electron transfer also produces oxygen as a by-product released during respiration. The cell can then use the ATP generated from photophosphorylation for energy-dependent processes, such as cellular growth and repair. Photosynthesis is, therefore, essential for life on Earth, as it provides the necessary energy for all living organisms. Plants are the key producers of oxygen on Earth, and the photosynthesis process is responsible for the majority of the oxygen in our atmosphere. Without photosynthesis, life on Earth would not be possible. Plants are essential for a healthy environment and a sustainable future. Without photosynthesis, our planet would be unable to sustain life. Therefore, preserving and protecting plants is essential for our future (Figure 4) [4].

The reaction centre is the pivotal part of photosynthesis, where the biological activities of converting light into chemical energy for the development of plants and photosynthetic bacteria commence. The initial stage in this process is the absorption of photon energy by the chlorophylls of the collecting antennas. This absorbed energy triggers the production of electron carriers in the reaction centre. The electron carriers move the electrons through the photosynthetic membrane, producing the energy required for metabolic processes. This energy is then used in the Calvin cycle to convert carbon dioxide to carbohydrate molecules such as glucose. Finally, these molecules are used for respiration and other metabolic processes, enabling plants to produce energy and grow. This process is known as photosynthesis and is essential for all living organisms' survival, as it is the primary energy source for most ecosystems. Photosynthesis is a complex process involving several molecular and biochemical reactions [9].

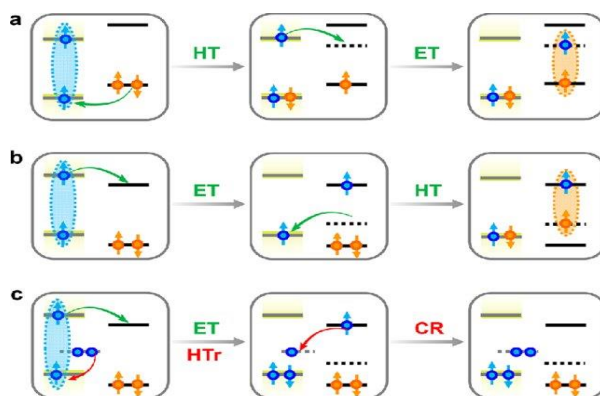
### 3.4. General reminder on the mechanisms of energy and electron transfer

When a sensitizing chromophore is present, two types of electron transfers occur, as shown in Figure 5. These are known as Dexter and Förster mechanisms. Dexter involves an energy transfer from the donor to the acceptor, while Förster involves an energy transfer from the acceptor to the donor. Both are important in the process of photosynthesis. The Dexter mechanism is the most efficient, requiring less energy and transferring more quickly. However, Förster is still important to the overall process of photosynthesis. The Förster mechanism is less efficient, but it allows for a longer distance between the donor and acceptor, allowing for more molecules to be involved in the photosynthetic process. The energy transfer can be Dexter or Förster (Figure 6) [10].



### 3.5. The transfer of electrons of the reducing or oxidizing type

When light is shone on a photosensitizing chromophore P, an electron is moved from a filled orbital to an empty orbital of higher energy, taking the molecule from its original or ground state to its excited state. This means that when in its excited state, the molecule can act as both an oxidizing and reducing agent. As a result, this increases the rate of certain chemical reactions that can carry out useful functions. This is the basis of photosynthesis, the process by which plants convert light energy into chemical energy. The energy produced by photosynthesis is then stored in the form of carbohydrates, which provide energy and raw materials for other metabolic processes. Photosynthesis is essential for all life on Earth, as it is most organisms' main energy source. Plants also use photosynthesis to produce the oxygen necessary for other organisms to breathe. Photosynthesis is thus a vital part of the global ecosystem and is essential for maintaining the life balance on Earth.

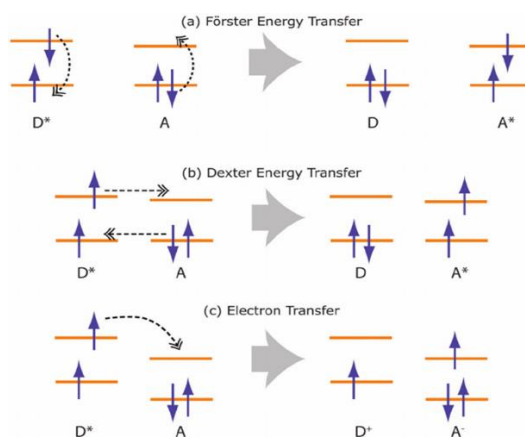


**Figure 5:** Trapping of the excited state of a photosensitizing chromophore P\* by reductive or oxidizing electron transfer [14]

There are, therefore, two types of electron transfer from P\*. The first is a so-called reducing electron transfer, shown in Figure 5 case (a): when their omophorion P is excited in P\*, the latter can accept an electron from a trapper rich in electrons. In this first case, P\* acts as an oxidizing agent; it is then reduced, hence the name of reducing electron transfer. In the second case, the electron transfer is said to be oxidizing, shown in Figure 5 case (b): in this case, the electron on the highest energy orbital of the excited chromophore P\* can be transferred to a trapper A poor in electrons. The chromophore P\* then plays the role of reducing agent, and it is oxidized, hence the name oxidizing electron transfer. Therefore, the type of electron transfer that occurs depends on the nature of species A that interacts with the P\* chromophore.

### 3.6. The transfer of energy of the Förster or Dexter type

When the transfer of excited state is carried out by transfer of energy, it does not induce a transfer of electrons in overall balance, and it, therefore, does not lead, in a net balance, to oxidation or reduction such as electron transfer. [11] There are two types of energy transfer: the first is called Dexter type (Figure 6, case a), and the second is called Förster type (Figure 6, case b).



**Figure 6:** Trapping of the excited state of a D\* donor chromophore by an acceptor chromophore A by energy transfer type (a) Dexter or (b) Förster [14]-[16]

The energy transfer occurs here so that chromophore  $D^*$  returns to its ground state  $D$  while simultaneously, the acceptor trapper  $A$  passes into its excited state  $A^*$ . In the case of a Dexter-type energy transfer, an electron exchange occurs from the  $S\ 1(D)$  state of  $D^*$  to the  $S\ 1(A)$  state of  $A$ , and a simultaneous electron exchange occurs from the  $S\ 0(A)$  state of  $A$  to the  $S\ 0(D)$  state of  $D^*$ . This double exchange of electrons requires a very strong covering of the  $D$ - $A$  orbitals; that is,  $D^*$  and  $A$  must be in close contact. This mechanism, therefore, works at short distances ( $< 10\ \text{\AA}$ ) or by collision. Conversely, Förster energy transfer does not require electron exchange; in this case, it is a dipole-dipole interaction through space, according to a Colombian mechanism. The excited state of the oscillating dipole  $D^*$  then creates an electrostatic field that produces the activation of  $A$  into  $A^*$  when  $D^*$  deactivates. Here, overlapping the  $D$ - $A$  orbitals is unnecessary, which allows the two chromophores to be separated by relatively large distances, from 10 to 100  $\text{\AA}$  [12].

#### **4. Excitonic coupling between two chromophores.**

During the irradiation of a chromophore, an electron is excited to a higher energy state. During this excitation, the chromophore switches to an electronic configuration where the promoted electron half fills the vital orbital, which was of higher LUMO energy in the ground state, while the HOMO orbital it left is half empty. This new excited state of the chromophore can be considered a dipole or an oscillator called an exciton. This exciton exerts an electrostatic influence on its surroundings. When several chromophores are in an appropriate proximity and configuration, the excitonic model considers and describes their resonant interaction between coupled excited states. Several mathematical treatments make it possible to describe this interaction, depending on the force with which these excited states are coupled and according to the nature of the excitons considered. Only the aspect related to the coupling of two excitons will be presented here for simplicity to understand the spectral variations associated with the presence of strong excitonic coupling and weak excitonic coupling.

The excitonic coupling between two identical chromophores results from the interaction between the dipoles formed in these chromophores during the promotion in each of them of an electron to an excited orbital. In strong coupling, this interaction lifts the degeneracy between the HOMO and LUMO orbitals, respectively identical to the origin for the two chromophores, similar to a dimer. This degeneracy release consequently modifies the energies of the interorbital transitions and, therefore, the absorption bands' characteristics in the molecule's UV-visible spectre. For this excitonic coupling to be possible, these two chromophores must be in relative proximity. The spectral variations linked to the presence of coupling between excitons will depend on their respective arrangement with each other. Three borderline cases have been studied in the literature [13] corresponding to geometric arrangements defined between the two chromophores:

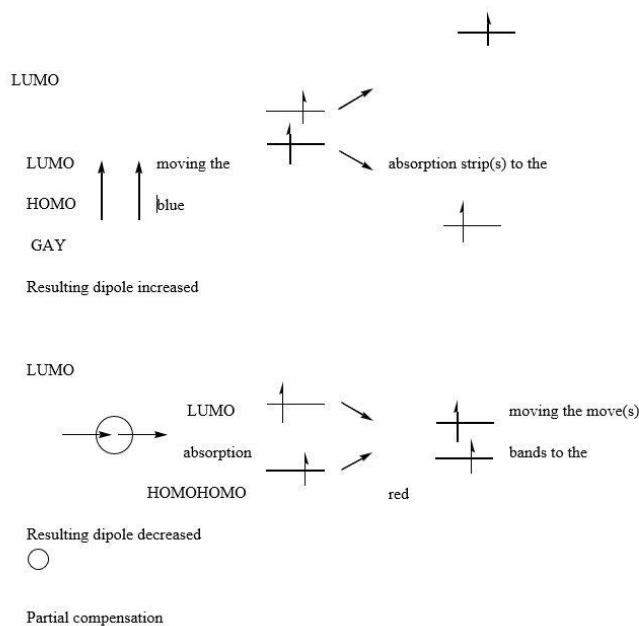
#### **5. Parallel arrangement of dipoles**

##### **5.1. Head-to-tail layout - Oblique layout**

The analysis of these three provisions presupposes the study of the energy variations of the orbitals involved, as well as the determination of the rules for selecting possible new transitions (i.e., identifying permitted and prohibited transitions). The theoretical studies in these three provisions lead to different effects in the UV-visible absorption spectrum and are summarised below.

##### **5.2. The parallel arrangement of the dipoles displaces the absorption bands of the UV- spectrum**

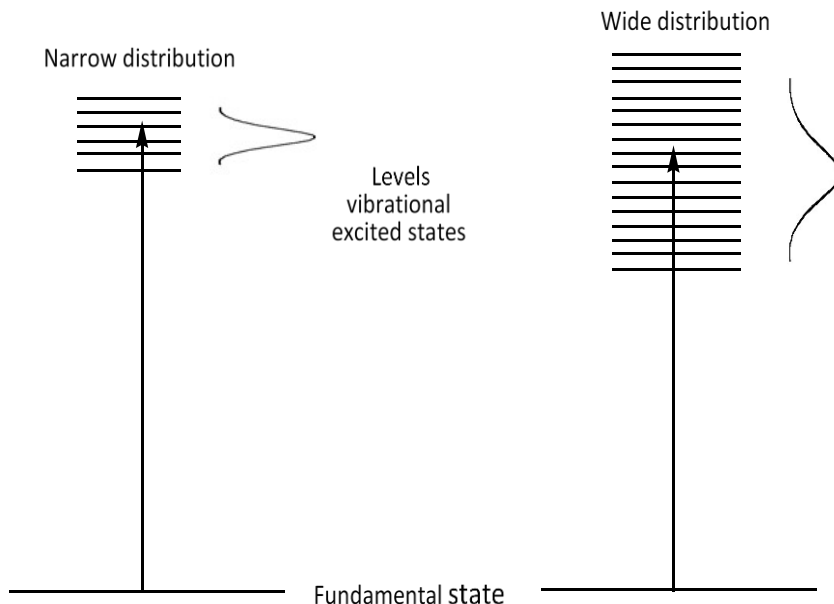
Visible towards stronger energies (towards blue). On the contrary, the head-to-tail arrangement shifts the bands of the spectrum to lower-energy transitions (towards red). These two scenarios are shown schematically in Figure 7. In the last case, the oblique arrangement of the dipoles leads to the duplication of the spectral bands on either side of the maximum absorption observed in the absence of coupling, a bit like a coupling of spins in NMR. As we mentioned previously, these cases correspond to strong couplings between excitons.



**Figure 7:** Excitonic coupling between two chromophores [20]

In the case of weak excitonic coupling, it is essentially manifested by a change in the shape of the absorption bands (Figure 8), such as an enlargement of the absorption band or a decrease in its intensity. Förster [13] described the two boundary situations for a porphyrin dimer connected by a bridge of variable length. The following effects are observed:

If the bridge molecule is long, the distance between the two chromophores is large, making the system more flexible.



**Figure 8:** The illustration of the widening of the Soret band due to weak excitonic coupling [20]

This flexibility leads to a wider distribution of the energies allowed for excited states, i.e. a wider range of possible transitions to the excited state. This resulted in the widening of the Soret Strip. If the bridge molecule is short, the chromophores come closer, and they are less mobile than in the case of a long bridge molecule: the system becomes more rigid. This rigidity decreases the number of possible transitions to the excited state, and thus, the Soret band becomes narrower than when the bridge molecule is longer.



Another explanation for the effect of excitonic coupling between two chromophores has been proposed by Dexter [14] in the case of chromospheres separated by a short distance. Indeed, they proved that Kasha's theory described this phenomenon well when the distance separating the two chromophores was greater than their dimension, but to describe the effects of excitonic coupling for lower separations, another approach was necessary. They interpreted this coupling using the Gouterman orbital model for porphyrins. This interpretation, called the treatment of the transition-monopole, considers the non-equivalence of the two polarized components (x and y) of the Soret and Q bands during the proximity of these two chromophores generated by electronic interactions between particular atoms. These components correspond to transitions on degenerate orbitals when porphyrins are in monomer form. In order to be able to study the interactions between chromophores and trappers and thus succeed in modelling natural photosynthetic systems, it is necessary to synthesize molecules with identified and appropriate physical and photochemical properties. Many research groups around the world are therefore interested in the development of multi-porphyrin systems.

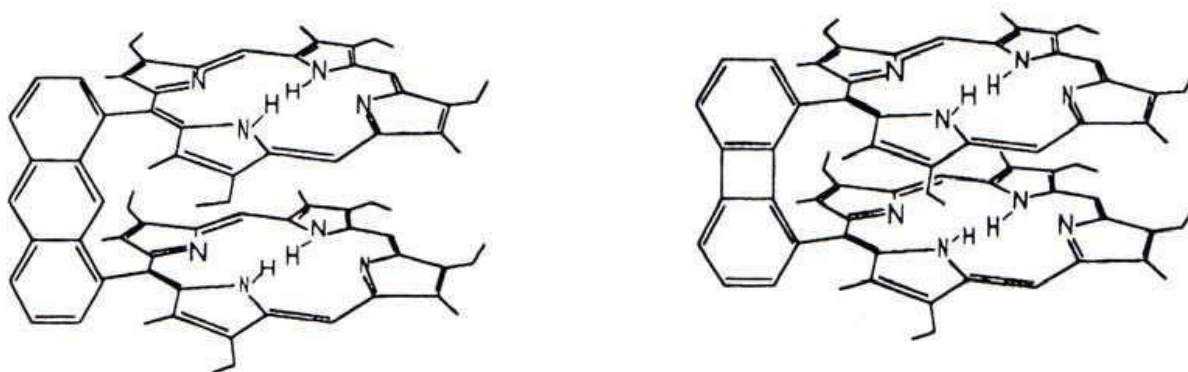
## 6. Porphyrins and Applications

Many efforts have been made to mimic CR's electron transfer process. Thus, many works related to the design and synthesis of artificial buildings, modelling by the nature and arrangement of their constituents' certain parts of the CR, have already been carried out. Thus, conjugated porphyrin-peptides have been developed as models for normal systems [14], and many chemists interested in imitating these systems have constructed artificial macrocyclic rows, usually through covalent bonds.

Tetrapyrrolic macrocycles have proved to be of great interest in many research areas such as molecular detection, molecular ideation, medicine (photodynamic therapy, nuclear boron capture therapy, and DNA cleavage), and optical applications (data storage nonlinear optical system, electrochromism, etc...). In Revanche, non-covalent synthesis based on self-assembly has emerged as a flexible alternative to covalent synthesis and offers the easy and fast construction of huge multi-porphyrin architectures. The coordination has a metal, and the hydrogen bonds have the most useful interactions for self-assembly. Many examples of multi-porphyrin architectures through these interactions have been reported.

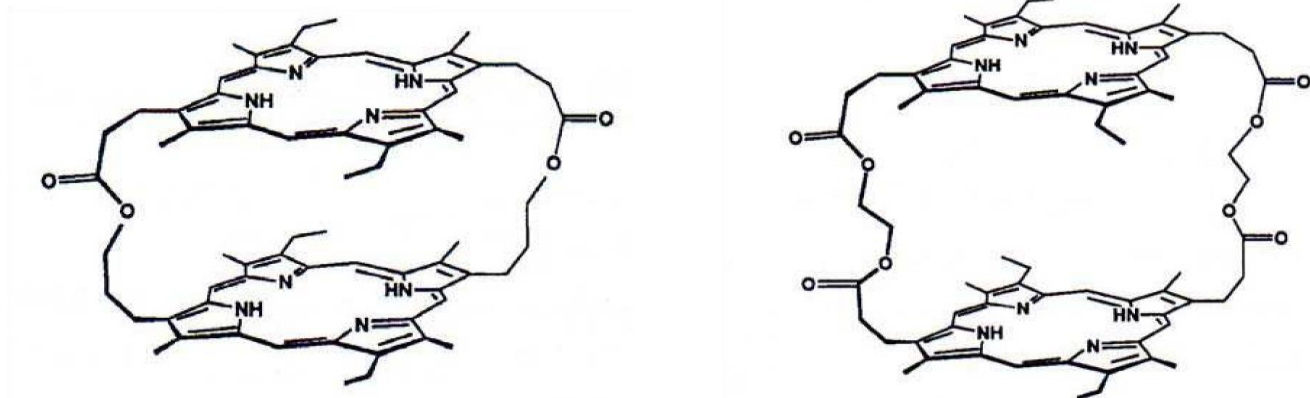
Thus, Juris et al., [15] synthesised the first cofacial porphyrins. Bridges in the meso position connect them and have the reduction of O<sub>2</sub> on graphite electrodes for application. Since then, many other cofacial bis-porphyrins have been synthesized for various applications [17].

Bencosme et al., synthesized in 1983 a facial bis-porphyrin with anthracene rigid spacer having activity for the lytic electrocatalytic reduction of oxygen on a graphite electrode [16]. In 1984, he expanded his work by demonstrating the same type of catalytic activity for a biphenylenediporphyrin. The two molecules are shown in Figure 9 [21]-[24].



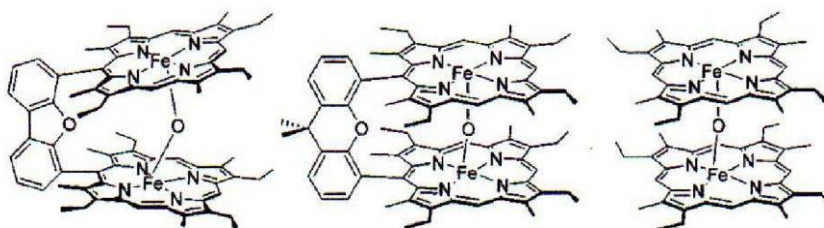
**Figure 9:** demonstrating the same type of catalytic activity for a biphenylenediporphyrin [24]

Hunter et al., [23] published in 1990 a facial bis-porphyrin for which the parallel position of the two porphyrins between them is ensured by two flexible diester junctions positioned in trans on each porphyrin. It demonstrates the formation of a host/receptor complex by complexation a DABCO molecule within the bis-porphyrinic cavity (Figure 10).



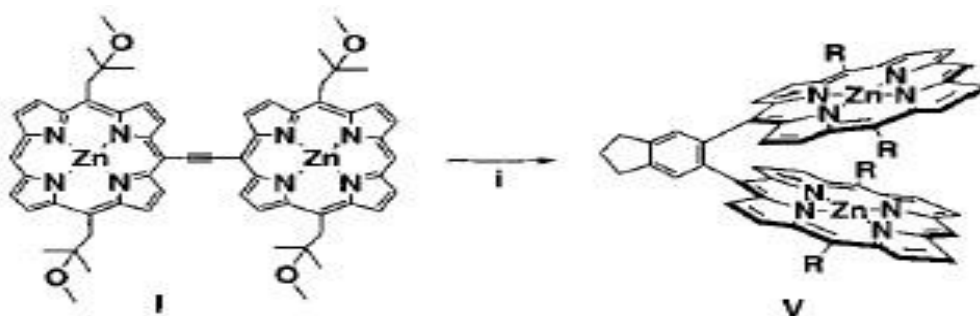
**Figure 10:** Demonstrates the formation of a host/receptor complex by complexation a DABCO molecule within the bis-porphyrinic cavity [25]

In 1992, Collman et al. [24] published the characterization of cofacial porphyrin dimer superoxide complexes of Co(II). In 2002, Pistorio et al., studied aerobic catalytic oxidation of Fe(II) bis-porphyrins with xanthene and dibenzofuran spacers (Figure 11) [25].



**Figure 11:** Aerobic catalytic oxidation of Fe(II) bis-porphyrins with xanthene and dibenzofuran spacers [26]

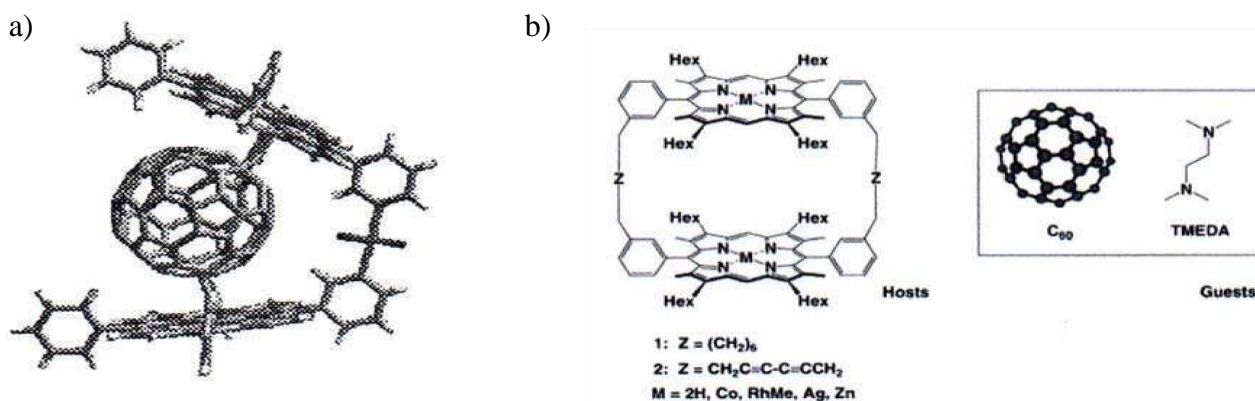
Solladié et al., published a new type of porphyrin supramolecular complex. An *o*-dioxymethylphenyl spacer connects two porphyrins to form a cofacial bis-porphyrin capable of complexing by  $\pi$ -stacking interactions with different nucleosides [17]. Therien published 2000 an elegant way to synthesize cofacial bis-porphyrins from linear bis-porphyrins with acetylenic spacer by cycloaddition reaction with 1,6-heptane (Figure 12) [27].



(i) I (67  $\mu$ mol), 1,6-heptadiyne (670  $\mu$ mol),  $\text{Co}_2(\text{CO})_8$  (134  $\mu$ mol), (87%)

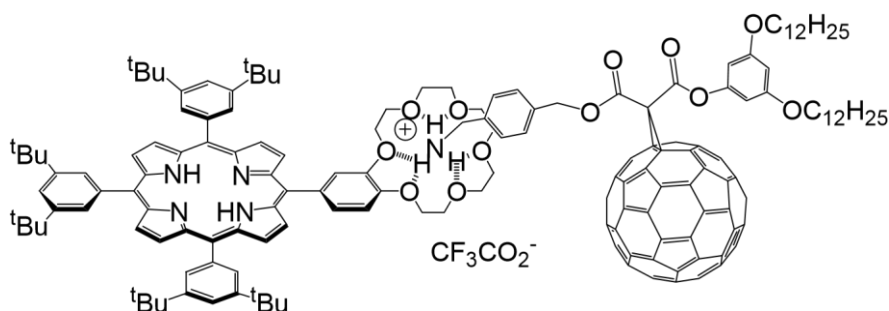
**Figure 12:** Bis porphyrins from linear bis-porphyrins with acetylenic spacer by cycloaddition reaction with 1,6-heptane [27]

Thallaj uses four hydrogen bond networks between two porphyrins substituted by four carboxylic acid functions to form a new cofacial porphyrin dimer [18]. Also, at the same time, porphyrin dimers for the complexation of  $\text{C}_{60}$  (Figure 13).



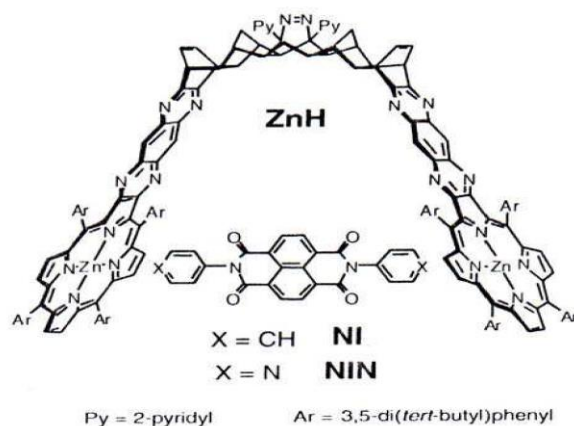
**Figure 13:** porphyrin dimers for the complexation of C60 [28]

Suppose the former uses the complexation of two pyridine substituents of porphyrins on Pd(II) to make their dimer. In that case, Aida prefers the covalent pathway by connecting the two chromophores by two junctions located in trans on each porphyrin. The laboratory obtained a supramolecular complex between a porphyrin bearing an ether-crown group with an ammonium-substituted C 60 derivative. An increase of two orders of magnitude in the association constant was observed (compared to the association between a single benzo-ether-crown and the same C60/ammonium derivative) due to the presence of  $\pi$ - $\pi$  interaction between the sphere of C60 and the aromatic ring of porphyrin, C60 being located just above the plane of porphyrin (Figure 14).



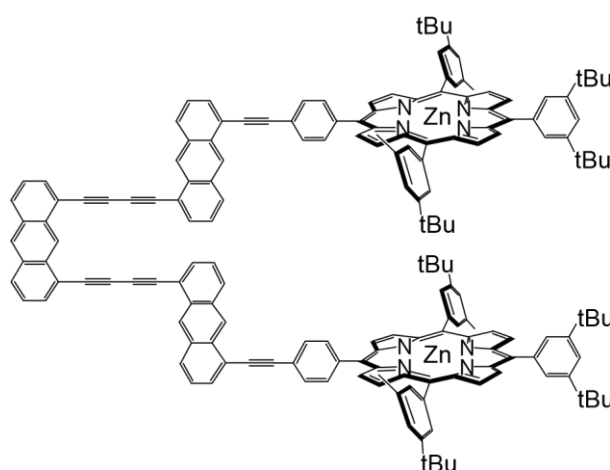
**Figure 14:** Porphyrin binds with fullerenesC60 [29]

Flamigni and Johnston study a photo-induced electron transfer within a supramolecular complex formed by a bis-porphyrinic receptor and a naphthalene diimide host (Figure 15) [28].



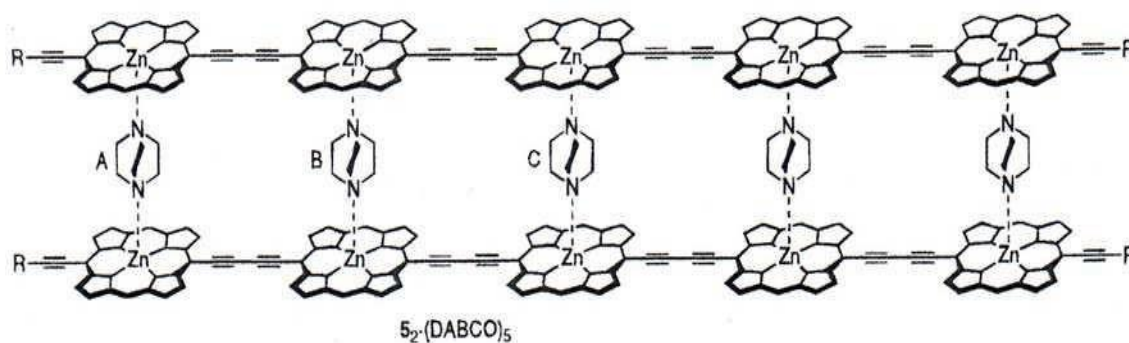
**Figure 15:** Structure of a bis porphyrin ZnH and the NIN and NI hosts [30]

Some extended forceps, consisting of two porphyrins connected by a tris-anthracene spacer, was synthesized in the laboratory. The presence of acetylenic junctions allows a free rotation along these triple bonds while maintaining a cofacial orientation of the porphyrins between them, thus constituting an adjustable cavity capable of accommodating hosts of varying sizes. Cavity adjustment has been demonstrated through the complexation of Lewis bidentate bases of various sizes (Figure 16). These complexes have been employed to recognise small molecules, such as amino acids and nucleosides, in aqueous media. Furthermore, the ability of the cavity to adjust to the size of substrates has enabled the capture of large molecules, such as proteins. This has helped to expand the scope of the applications for this technology since a wide variety of substrates can be captured. This has opened up new opportunities for research in biotechnology, drug discovery, and diagnostics. This has led to a surge in interest in the area and a rapid increase in funding for research into the uses of this technology. As a result, several new products and applications are being developed that could revolutionize the medical and biotechnology sectors. These products and applications could have a dramatic impact on the way we diagnose and treat diseases, as well as on the way we monitor and manage our health. This could vastly improve patient outcomes and healthcare services.



**Figure 16:** Work of N. Solladié for synthesising an adjustable cavity clamp [31]

In 1999, Taylor and Anderson published their work on oligomers porphyrinic metallated with Zn (II) and their complexation (Figure 17) [30].



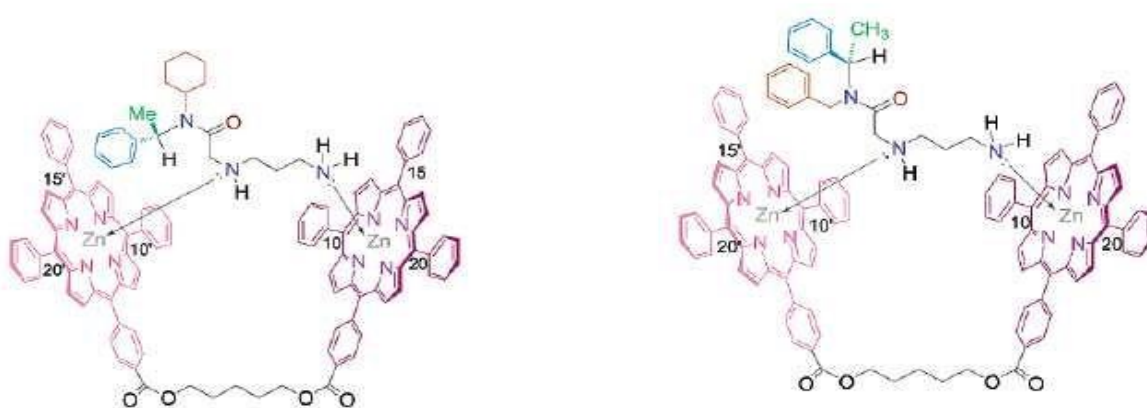
**Figure 17:** Pentamers metallated with Zn (II) are complexed by 5 DABCO, hence the nomenclature [32]

Thallaj worked on porphyrinic oligomers of Zn(II) ranging from dimer to hexamer. These oligomers form stable scale-shaped complexes, thanks to bidentate bases such as 1,4-diazabicyclo [2,2,2] octane (DABCO) and 4,4'bipyridine (Bipy). Titrations by UV-visible spectroscopy proved the structure and stability of these double porphyrine chains forming a scale. They worked mainly on DABCO because its basicity makes it possible to obtain stable complexes. The complexations showed that in excess DABCO, the "scales formed" could dissociate to give simple molecular threads always coordinated by the complexant. However, as the length of the multi-porphyrinic threads increases, the stability of the supramolecular complexes formed is increased, and it is increasingly difficult to associate them. The formation of scales increases the planarity of complexes and, thus, the conjugation of molecular systems [19].

In addition, the scales formed can absorb visible light, making them suitable for optoelectronic materials. This increases their potential applications in fields such as photovoltaics and sensors. These materials can also be used in displays, lasers, and light-emitting diodes. Furthermore, their properties can be tuned by controlling the size and shape of the nanostructures. This makes them highly versatile and customizable for different applications. As such, these nanostructures have great potential for use in various industries. Research into nanostructures is ongoing, and new and improved materials are expected to be developed in the future. This could lead to even more applications of these materials in various industries, allowing them to be further exploited. This will help to revolutionize these industries' operations, resulting in better products, more efficient processes, and, ultimately, higher profits.

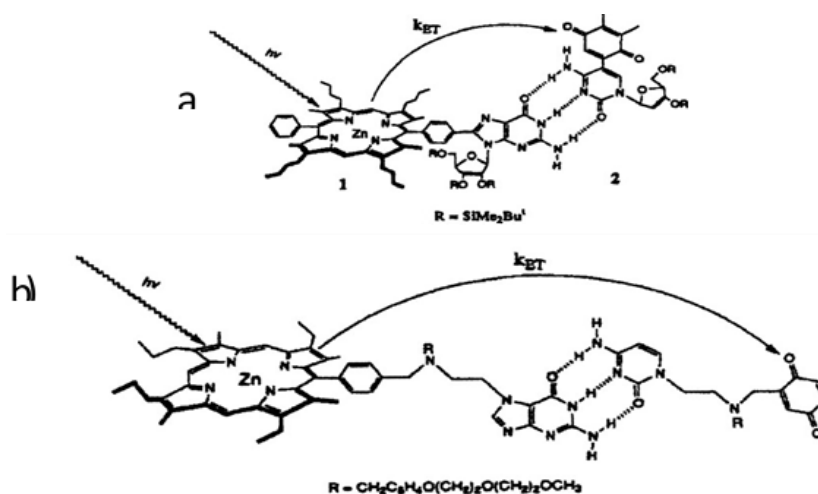
Borovkov et al., is interested in supramolecular chirogenesis thanks to a dimer of porphyrins with bis-methylene spacer, to which the absolute configuration of the host enantiopur imposes a chiral character [31].

Förster [13] uses a dimer of cofacial Zn (II) porphyrins with a flexible spacer to determine the absolute configuration of complexed hosts Figure 18.



**Figure 18:** Determining the absolute configuration of amines using a porphyrin dimer [33]

In 1992, Sessler et al. were able to establish a system in which zinc porphyrin (photodonor) is attached with a benzoquinone (acceptor) in three (non-covalent) Watson-Crick hydrogen bonds [34] (Figure 19, a). It wasn't easy to know whether a transfer of energy took place because of the non-rigidity of the system. A year later, another more rigid system could be developed for trapping the emission of zinc porphyrin (Figure 19, b).

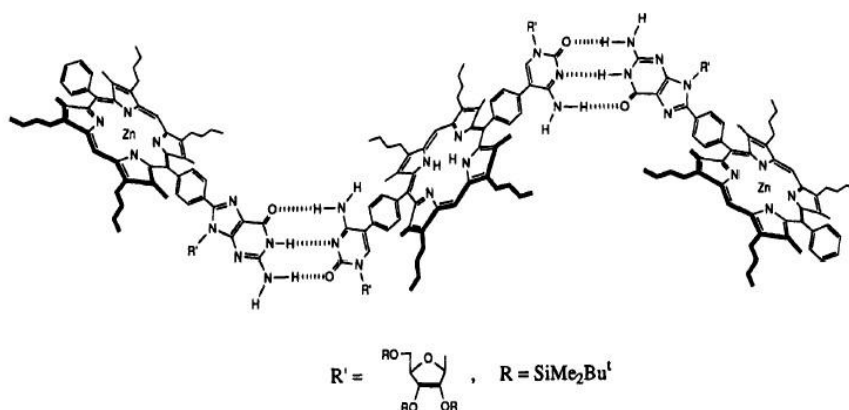


**Figure 19:** Non-covalent systems [33]



This system was stable enough to study the energy transfer between the donor and acceptor. It allowed them to show that energy transfer was indeed occurring between the two molecules. They observed that the energy was very efficient and transferred over a long distance. This breakthrough was a great step toward understanding energy transfer in molecular systems. This research provided important insight into the nature of energy transfer and how it can be used to design efficient systems for energy harvesting. It could hold the key to new, more efficient energy harvesting methods. This could lead to advances in renewable energy sources such as solar and wind power and new ways to store energy. It could also open up a new field of research into energy transfer in molecular systems [22].

In 1995, the same group published an example of tris-porphyrin having rigid conformation through hydrogen bonds, Figure 20. This structure was used as a model for studying the intramolecular forces of the porphyrins. The results showed that the hydrogen bonds were the main factor in stabilising the rigid conformation.



**Figure 20:** Tris-porphyrin Zn<sub>2</sub> [33]

This was a breakthrough in understanding the chemistry of porphyrins. This knowledge can be applied to create new molecules with improved properties for various applications. For example, it has already been used to create molecules with enhanced drug delivery. Additionally, it has allowed scientists to understand how to manipulate the structure of molecules for better performance. This has enabled the design of new materials with higher efficiency and durability. It has also been used to develop new, more effective catalysts for industrial processes. Overall, this knowledge can potentially revolutionise how we approach molecules and catalysts. It can potentially lead to discoveries and breakthroughs in many fields [23]. This could lead to more efficient and less expensive manufacturing processes, allowing us to build and create more sustainable products. It can also help reduce waste and pollution, improving our environment and the health of our planet [34]-[35].

## 7. Conclusion

The bis-porphyrin nucleoside spacer system is an effective tool for molecular recognition, allowing for selective binding of target molecules. Its use in various biological and chemical applications is promising, and more research is needed to explore its potential. Currently, the system is being used in drug delivery, biosensing, and bioconjugation. It has also been used to create fluorescent imaging probes and detect small molecules. Further research is needed to understand the full potential of this system. For example, it has been used to create nanocarriers for drug delivery, which can target specific body areas with greater accuracy. It has also been used to detect small molecules, such as cancer biomarkers, which could help in early diagnosis of diseases. Research is also ongoing to explore its potential in gene delivery, tissue engineering, and other applications. Ultimately, the potential of this system is vast and could revolutionize how we approach medical treatments. The system has already been successfully tested in clinical trials and is being further developed for use in humans. The technology has the potential to revolutionize the way we approach healthcare and could lead to a significant improvement in patient outcomes. This could make treatments more efficient and affordable and revolutionize the healthcare industry. This system could be used to treat a wide range of conditions, from genetic disorders to cancer. This technology could be a game-changer for healthcare, potentially drastically reducing healthcare costs and improving patient outcomes. It could also open up new avenues of research, paving the way for developing more effective treatments for a wide range of conditions.

At the same time, this technology could be used for unethical purposes. It could be used to create genetically modified organisms for military and commercial purposes, or it could be used to create designer babies. Therefore, it is important to regulate the



use of this technology to ensure that it is used only for ethical purposes. There is also a potential risk of the technology being abused by corporations and governments. This could lead to further exploitation and discrimination of vulnerable populations. It is, therefore, essential to have robust safeguards to protect against these potential abuses. Regulatory bodies should be established to monitor the use of this technology and ensure that it is used responsibly. Companies should also be held accountable for their actions and be required to have ethical policies in place. Finally, public education and awareness should be implemented to ensure that people are aware of the risks of this technology. Consumers should also be empowered to make informed decisions about the use of this technology by providing information about the risks and potential abuses. Governments should also work to ensure the legal framework is in place to protect individuals from potential abuses. Companies should also be held accountable for any misuse of the technology, and penalties should be put in place to discourage irresponsible use.

Governments should also invest in research to assess the potential long-term impacts of this technology. Finally, a system should be in place to monitor and regularly review the use of this technology. Education and public awareness should be part of the plan to ensure citizens are informed of the potential risks and to ensure ethical use. Regular audits should be conducted to ensure that companies are abiding by the law. Finally, an independent regulatory body should be established to ensure the technology is used responsibly. Strict penalties should be in place for companies that violate the regulations, which should be enforced to ensure compliance. Additionally, companies should be encouraged to invest in more secure systems and safeguards to protect citizens' data from misuse. Companies should also be held accountable for any data breaches that occur and should be required to notify affected customers immediately. Finally, governments should pass laws to protect citizens' data and privacy from misuse. Companies should be required to report any suspicious activity to the government and the relevant authorities. They should also be held responsible for any damage caused by data breaches or other misuse of personal data. Furthermore, companies should be required to have clear and transparent policies regarding the collection, use and storage of personal data.

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## References

1. T. Pullerits and V. Sundström, "Photosynthetic light-harvesting pigment– protein complexes: toward understanding how and why," *Accounts of Chemical Research*, vol. 29, no. 8, pp. 381–389, 1996.
2. R. Heller, *Physiologie végétale*, 1981, p. 153, Ed. Masson, USA. ISBN 2-225 68387-5.
3. R. Huber, "A structural basis of light energy and electron transfer in biology (Nobel Lecture)," *Angewandte Chemie International Edition in English*, vol. 28, no. 7, pp. 848–869, 1989.
4. J. Deisenhofer and H. Michel, "The photosynthetic reaction center from the purple bacterium *Rhodospseudomonas viridis* (Nobel lecture)," *Angewandte Chemie International Edition in English*, vol. 28, no. 7, pp. 829–847, 1989.
5. J. Deisenhofer, O. Epp, K. Miki, R. Huber, and H. Michel, "X-ray structure analysis of a membrane protein complex: electron density map at 3 Å resolution and a model of the chromophores of the photosynthetic reaction center from *Rhodospseudomonas viridis*," *Journal of molecular biology*, vol. 180, no. 2, pp. 385–398, 1984.
6. J. Deisenhofer, O. Epp, K. Miki, R. Huber, and H. Michel, "Structure of the protein subunits in the photosynthetic reaction centre of *Rhodospseudomonas viridis* at 3Å resolution," *Nature*, vol. 318, no. 6047, pp. 618–624, 1985.
7. G. McDermott et al., "Crystal structure of an integral membrane light-harvesting complex from photosynthetic bacteria," *Nature*, vol. 374, no. 6522, pp. 517–521, 1995.
8. W. Kühlbrandt, "Many wheels make light work." *Nature* 374, no. 6522: 497-498, 1995.
9. H. Zuber, "Structure of light-harvesting antenna complexes of photosynthetic bacteria, cyanobacteria and red algae," *Trends Biochem. Sci.*, vol. 11, no. 10, pp. 414–419, 1986.
10. P. A. Simone and R. Bullough, "The 8.5 Å projection map of the light-harvesting complex I from *Rhodospirillum rubrum* reveals a ring composed of 16 subunits," *The EMBO journal*, vol. 14, no. 4, pp. 631–638, 1995.

11. R. F. Stefan and S. G. Goldstein, "Distance dependence of electron-transfer reactions in organized systems: the role of superexchange and non-Condon effects in photosynthetic reaction centers," *The Journal of Physical Chemistry*, vol. 97, no. 12, pp. 3040–3053, 1993.
12. J. R. Kazimierz, V. Diers, J. P. Chynwat, H. A. Erickson, and D. F. Frank, "Characterization of the strongly coupled, low-frequency vibrational modes of the special pair of photosynthetic reaction centers via isotopic labeling of the cofactors," *Journal of the American Chemical Society*, vol. 119, no. 2, pp. 415–426, 1997.
13. T. Förster, "Zwischenmolekulare energiewanderung und fluoreszenz," *Ann. Phys.*, vol. 437, no. 1–2, pp. 55–75, 1948.
14. D. L. Dexter, "A theory of sensitized luminescence in solids," *J. Chem. Phys.*, vol. 21, no. 5, pp. 836–850, 1953.
15. A. Juris, V. Balzani, F. Barigelletti, S. Campagna, P. L. Belsler, and A. Von Von Zelewsky, "Ru (II) polypyridine complexes: photophysics, photochemistry, electrochemistry, and chemiluminescence," *Coordination Chemistry Reviews*, vol. 84, pp. 85–277, 1988.
16. D. Jr, C. S. Bencosme, J. P. Collman, and F. C. Anson, "Mechanistic aspects of the catalytic reduction of dioxygen by cofacial metalloporphyrins," *Journal of the American Chemical Society*, vol. 105, no. 9, pp. 2710–2718, 1983.
17. N. Thallaj, "Quick Review of Chemistry Related to the [Fe]- Hydrogenases," *International Journal of Advanced Pharmaceutical Sciences and Research*, vol. 4, pp. 1–15, 2021.
18. P. D. N. Thallaj, "Review of a few selected examples of intermolecular dioxygenases involving molecular oxygen and non-heme iron proteins," *International Journal of Advanced Pharmaceutical Sciences and Research*, vol. 3, no. 2, pp. 1–18, 2023.
19. P. D. N. Thallaj, "A short review of some examples of the binding of fullerenes C60 to transition metal complexes," *International Journal of Advanced Pharmaceutical Sciences and Research*, vol. 2, no. 6, pp. 1–12, 2022.
20. P. D. N. Thallaj, "A brief overview of the general characteristics and reactivity towards dioxygen of the ferrous Tris (2-pyridylmethyl Amine) series complexes is presented," *International Journal of Advanced Pharmaceutical Sciences and Research*, vol. 3, no. 3, pp. 1–10, 2023.
21. C. K. Chang and I. Abdalmuhdi, "A Biphenylenediporphyrin: Two Cofacially Arranged Porphyrins with a Biphenylene Bridge," *Angew. Chem. Int. Ed. Engl.*, vol. 23, no. 2, pp. 164–165, 1984.
22. J. P. Collman, D. A. Tyvoll, L. L. Chng, and H. T. Fish, "Facile synthesis of meso-tetraaryl cofacial diporphyrins," *J. Org. Chem.*, vol. 60, no. 7, pp. 1926–1931, 1995.
23. C. A. Hunter, M. N. Meah, and J. K. Sanders, "Dabco-metalloporphyrin binding: ternary complexes, host-guest chemistry and the measurement of pi.-pi. interactions," *Journal of the American Chemical Society*, vol. 112, no. 15, pp. 5773–5780, 1990.
24. J. P. Collman et al., "Synthesis and characterization of a superoxo complex of the dicobalt cofacial diporphyrin, the structure of the parent dicobalt diporphyrin Co2 (DPB), and a new synthesis of the free-base cofacial diporphyrin H4 (DPB)," *Journal of the American Chemical Society*, vol. 114, no. 25, pp. 9869–9877, 1992.
25. B. J. Pistorio, C. J. Chang, and D. G. Nocera, "A phototriggered molecular spring for aerobic catalytic oxidation reactions," *J. Am. Chem. Soc.*, vol. 124, no. 27, pp. 7884–7885, 2002.
26. K. Tashiro and T. Aida, "π-Electronic Charge-Transfer Interactions in Inclusion Complexes of Fullerenes with Cyclic Dimers of Metalloporphyrins," *Journal of inclusion phenomena and macrocyclic chemistry*, vol. 41, pp. 215–217, 2001.
27. N. Solladié et al., "Supramolecular complexes obtained from porphyrin–crown ether conjugates and a fullerene derivative bearing an ammonium unit," *Tetrahedron*, vol. 62, no. 9, pp. 1979–1987, 2006.
28. L. Flamigni and M. R. Johnston, "Photoinduced electron transfer in a non-covalently linked donor-acceptor system: a bis-porphyrinic host and a naphthalene diimide guest," *New Journal of Chemistry*, vol. 25, no. 11, pp. 1368–1370, 2001.
29. R. Rein, M. Gross, and N. Solladié, "Adjustable cavity for host-guest recognition in cofacial bis-porphyrinic tweezer," *Chem. Commun. (Camb.)*, no. 17, pp. 1992–1993, 2004.
30. P. N. Taylor and H. L. Anderson, "Cooperative self-assembly of double-strand conjugated porphyrin ladders," *J. Am. Chem. Soc.*, vol. 121, no. 49, pp. 11538–11545, 1999.
31. V. V. Borovkov, M. Juha, and Y. Lintuluoto, "Supramolecular chirogenesis in bis (zinc porphyrin): an absolute configuration probe highly sensitive to guest structure," *Organic Letters*, vol. 2, no. 11, pp. 1565–1568, 2000.
32. X. Huang et al., "Absolute configurational assignments of secondary amines by CD-sensitive dimeric zinc porphyrin host," *J. Am. Chem. Soc.*, vol. 124, no. 35, pp. 10320–10335, 2002.
33. J. L. Sessler, B. Wang, and A. Harriman, "Long-range photoinduced electron transfer in an associated but non-covalently linked photosynthetic model system," *J. Am. Chem. Soc.*, vol. 115, no. 22, pp. 10418–10419, 1993.
34. A. Harriman, Y. Kubo, and J. L. Sessler, "Molecular recognition via base pairing: photoinduced electron transfer in hydrogen-bonded zinc porphyrin-benzoquinone conjugates," *J. Am. Chem. Soc.*, vol. 114, no. 1, pp. 388–390, 1992.
35. J. L. Sessler, B. Wang, and A. Harriman, "Photoinduced energy transfer in associated, but noncovalently-linked photosynthetic model systems," *J. Am. Chem. Soc.*, vol. 117, no. 2, pp. 704–714, 1995.