Poster 68

Laser based origami with protein films

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The traditional Japanese art of paper folding, origami, has inspired the design of innovative engineered devices and structures for decades. Examples of some of their applications include flat-folding rigid shopping bags, foldable shipping container, solid solar panel, 3D biomedical structures and robotics (1,2). More recently, the interest has turned towards the use of active materials that are capable of acting the desired folding behaviour in response to external stimuli (3,4).

This project involves a preliminary investigation into the properties of protein single-layer (gelatin and silk fibroin) films and how they may be manipulated in order to change their shape, or fold. This exciting new concept is incorporated into a patent (5). Based on a new class of tessellating origami folds, the films are fabricated via casting methods and precision engraved with ultra-fast lasers (nanosecond and femtosecond lasers) and then primed to assemble when triggered. Various trigger properties (solvent type, pH and temperature) are investigated to identify the optimum conditions for self-assembly. Our results show that silk fibroin films exhibit optimum folding upon the addition of ethanol due to molecular structure changes within the silk.

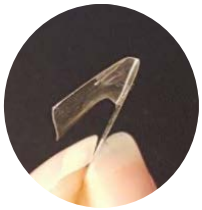

Figure 1. Folded silk fibroin film patterned with a femtosecond laser and triggered by ethanol.

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Poster 69

Transition Metal Oxide Photonics – Self Organization and Atomic Defects

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Transition metal oxides such as titanium dioxide (TiO_2) have been the focus of sustained investigation in applications such as photocatalysis and photonic material fabrication [1,2]. This study aims to elucidate some of the properties of these transition metal oxide systems, using electrochemically grown TiO_2 nanotubes, in enhanced Raman scattering and photocatalysis.

Healthcare, security, and chemical manufacturing are just some of the fields that have benefited from the development of Surface Enhanced Raman Spectroscopy (SERS). Recently, a technique known as Photo-Induced Enhanced Raman Spectroscopy (PIERS) [1] is poised to increase the sensitivity of SERS even further. However, despite its many advantages, PIERS still suffers from problems such as reproducibility and scalability. We use thermal de-wetting of silver nanoparticles on hexagonal titanium dioxide nanotubes to produce self-organized and reproducible nanoparticle distributions. We also perform an in-depth study of the electron transfer mechanisms giving rise to the PIERS effect, in order to understand the source of the enhanced Raman signal.

The other focus of this study is in TiO_2 's ability to degrade environmental pollutants and perform water splitting [1]. Due to TiO_2 's nature as a wide-bandgap semiconductor, photocatalysis only occurs with reasonable efficiency under ultraviolet irradiation. By patterning the surface of titanium with Laser Induced Periodic Surface Structures (LIPSS) prior to nanotube growth, we create a structure (LIPSSticks) that can trap visible light [3]. This is a double-self-organized growth process, as both the nanotubes and LIPSS grow in a self-organized manner to create the LIPSSticks. The enhanced visible light absorption is predicted via computational modelling and the morphological evolution of the anodization process was investigated. This study provides the basis for further work into LIPSS templating of other anodized transition metal oxide materials.

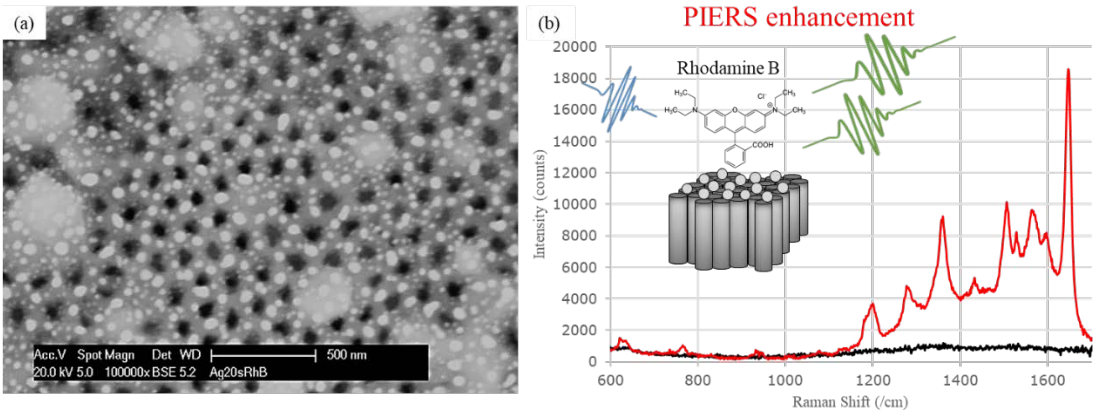

Figure 1 (a) SEM mages of TiO2 nanotubes with thermally-dewetted silver nanoparticles, (b) (Inset) Cartoon of PIERS spectroscopy of Rhodamine-B, PIERS spectrum of Rhodamine-B (red line), Non-enhanced spectrum (black) at 488 nm.

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Poster 70

Ni/TiO_2 - Low Cost Photocatalysts for Solar H_2 Production

Wan-Ting Chen
Geoffrey I.N. Waterhouse

This work targets the development of efficient metal co-catalyst modified titania photocatalysts for alcohol photoreforming to H_2 that function under direct sunlight.[1] Conventionally, noble metals such as platinum (Pt), palladium (Pd) or gold (Au) have been used co-catalysts to activate TiO_2 for hydrogen production, though the use of such co-catalysts for industrial scale H_2 manufacture is not feasible due to their high cost and low natural abundance, motivating the search for low cost alternatives.[2]

This study compares the performance of three different Ni/TiO_2 photocatalysts for H_2 production in alcohol-water mixtures, placing particular emphasis on the role of the TiO_2 support and alcohol sacrificial reagent. P25 TiO_2 (85 wt.% anatase, 15 wt.% rutile), isolate anatase from P25 TiO_2, isolate rutile from P25 TiO_2, commercial brookite and physical mixed P25 TiO_2 were used as the support phase. The Ni/P25 TiO_2 photocatalysts were very active for H_2 production in 10 vol.% alcohol-water mixtures under UV excitation, with the optimal Ni loading being ~0.5 wt.% (highest H_2 production rate = 26.0 mmol g^{-1} h^{-1} in 10 vol.% glycerol). Ni/anatase and Ni/physical mixed P25 photocatalysts showed a diminution in the photocatalytic H_2 production performance, which confirmed the importance of interfacial electron transfer at the rutile:anatase interface.

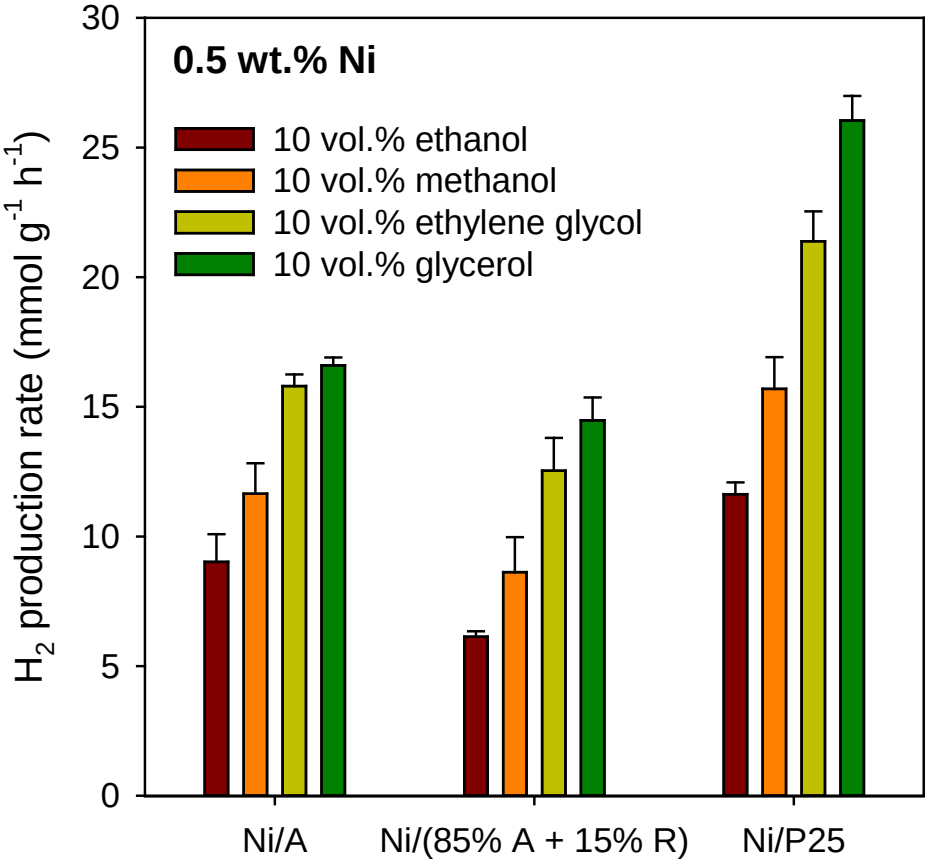

Figure 1. Plots of H_2 production for 0.5 wt.% Ni/TiO_2 photocatalyst prepared using different TiO_2 supports (A = anatase, R = rutile, P25 = 6:1 anatase:rutile).

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Poster 71

Improvement for Photoactivatable HNO Donors: Effects of a Simple Modification to the (Hydroxy-naphthalenyl)methyl Phototrigger

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HNO is a biologically relevant, highly reactive molecule that requires precursors to generate it in situ. The use of phototriggers to release HNO is attractive for kinetic and mechanistic studies of HNO's bioreactivity due to the rapid rate of HNO release upon light activation. We recently developed a novel class of photoactivatable HNO donors incorporating the (3-hydroxy-2-naphthalenyl)methyl (3,2-HNM) phototrigger together with the HNO-releasing N-hydroxysulfonamide moiety. A simple modification of the photocage to the 6,2-HNM analogue drastically improved the selectivity for the desired HNO-generating pathway. The photochemistry of 6,2-HNM photoprotected donor and model compounds has now been investigated using transient absorption spectroscopy, fluorescence spectroscopy, NMR and LC-MS photoproduct characterization, and UV/Vis absorption spectroscopy. Multiple photodecomposition pathways are accessible with the selectivity between the two major pathways being highly controllable by the pH of the aqueous component of the solution. Preliminary evidence suggests that the HNO donor has both a photoacidic and a photobasic site. The combination of these two sites may allow for the formation of a tautomer and consequently a decomposition pathway not otherwise accessible in the ground state under neutral pH conditions.

Poster 72

Towards Elucidating the Mechanism of the Copper-Catalysed Oxidative Cross-Coupling of P-H and N-H: Reaction Component Considerations and Mechanistic Evidence

J. Feld, Y. Ben-Tal
E. M. Leitao

Catalysis is central for the practical usage of chemical synthesis. In our modern awareness of energy consumption and waste disposal, the chemical industry relies heavily on catalytic reactions that feature low energy cost, high efficiency and high selectivity. In main group chemistry, catalytic formation of E-E' main group bonds from E-H with the elimination of hydrogen gas is called dehydrogenative coupling. In particular, copper salts have been reported to catalyse the formation of nitrogen-phosphorus bonds via a dehydrogenative coupling in the presence of air. Nitrogen-phosphorus bonds are usually synthesised in the lab from condensation reactions analogous to C-N bond formation. The absence of halogenated species and harsh reagents makes this reaction a potential candidate for large quantity production.

Copper salts are cheap and commercially available, but this reaction is slow compared to industrial standards, and homocoupling of the amine and phosphite makes selectivity an issue. In order to improve efficiency and yield we need to understand the intricacies in the mechanism. Our project consists of using documented techniques such as control reactions, kinetic monitoring, model reactions, and labelling studies to work towards postulating intermediates and transition states. Furthermore, we are comparing different starting materials and experimental conditions, in addition to focusing on the addition of base/ligands to investigate the electronics of the active copper catalyst.

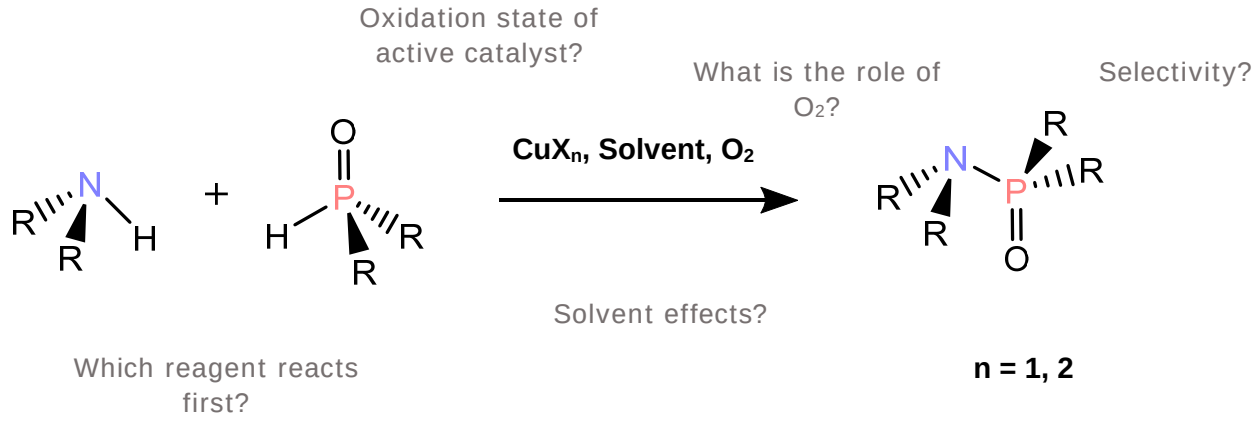

Figure 1. Copper Catalyzed Oxidative Cross Coupling of N-H and P-H

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2. a) Fraser, J.; Wilson, L. J.; Blundell, R. K.; Hayes, C. J. *Chemical Communications* **2013**, *49*, 8919-8921. b) Wang, G.; Yu, Q.-Y.; Chen, S.-Y.; Yu, X.-Q. *Tetrahedron Letters* **2013**, *54*, 6230-6232.

Poster 73

High Melt Strength, Tear Resistant Blown Film Based on Poly-lactic acid.

Vitalii Furt
Neil Edmonds, Dr. Jianyong Jin, Dr. Peter Plimmer

Current polymers used for blown film production are not biodegradable and non-compostable, which is undesirable from an environmental point of view. In light of depleting landfill space and stricter environmental laws, there is a need for biodegradable films.
Poly-lactic acid is considered as one of the most promising ecological, bio-sourced and biodegradable plastic materials. It's a highly versatile biodegradable polymer that can be modified for blown film manufacture and potentially replace traditional petroleum derived polymers.
Through reactive compounding with a number of materials, Poly-lactic acid is given the required mechanical properties. In reactive compounding, a chemical reaction proceeds under elevated temperature and high shear to covalently bond the components and results in a lightly cross-linked structure. The resulting polymer is tough, melt-stable, with improved mechanical properties; biodegradable, non-toxic, relatively nonvolatile, FDA approved, cost-effective and is easily processable on existing equipment for blown film manufacture.
A number of various additives can also be incorporated into the resin composition. These include fillers, antioxidants, light stabilizers, UV absorbing additives, lubricants, mold release agents, antistatic agents, pigments, flame retardants etc.

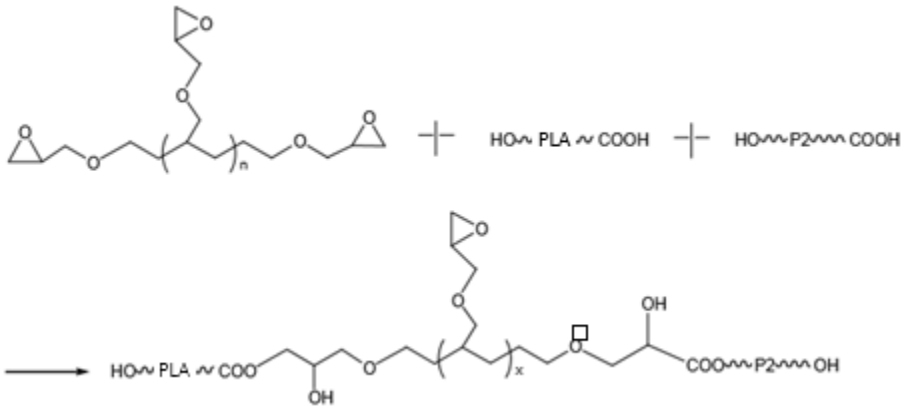

Figure 1. Proposed reaction between Poly-lactic acid and some of the components of the mixture.[1]

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Poster 74

NMR Toolkit for Fragment-based Inhibitor Screening

Renjie Huang, Ivanhoe Leung, Arnaud Bonnichon,

In a fragment screen, small 'fragment-like' molecules are used probes to investigate potential protein-ligand interactions [1]. These fragments, by nature, tend to bind weakly to the protein, and further development is required to order to develop them into higher affinity lead compounds.

Conventional biophysical tools are suitable to detect strong binders, such as those with a dissociation constant (K_D) in the pM to low µM region. Fragments, however, tend to bind with a K_D range of high µM to mM.

Nuclear magnetic resonance (NMR) has emerged a powerful tool for fragment screen. Protein-observe techniques such as the ^{1}H-^{15}N heteronuclear single quantum correlation (HSQC) experiment using isotopic labelled proteins is one of the most robust methods to characterise protein-ligand interactions[2]. However, it is not suitable for all protein systems due to cost[3]. Ligand-observe techniques including the water-ligand observed via gradient spectroscopy (waterLOGSY) and transverse relaxation (T_2)-edited method using the Carr-Purcell Meiboom-Gill (CPMG) sequence, on the other hand, may cover a smaller K_D range but they are capable of being used as a high throughput of screening method to screen mixtures of compounds[1]. Herein, we describe the use of these different NMR technique to aid fragment-based drug discovery.

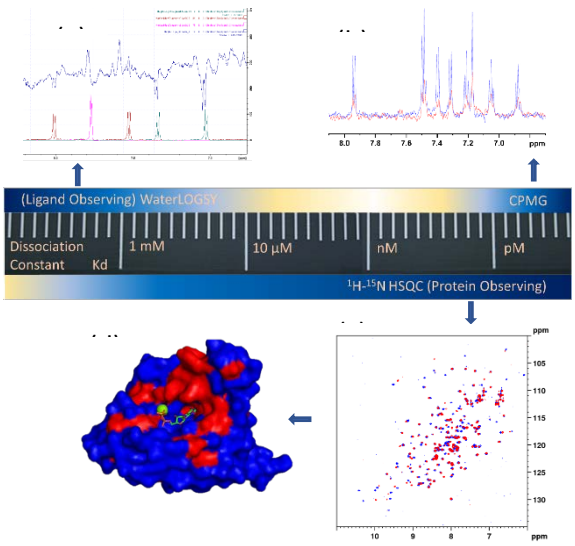

Figure 1 a). WaterLOGSY spectra of 3 fragments and a protein target. b). CPMG-edited 1H NMR showing the aromatic signals of a ligand decreases in the presence of a protein c). ^{1}H-^{15}N heteronuclear single quantum coherence (HSQC) spectra of ^{15}N-labelled HSP90-ND (blue) and ^{15}N-labelled HSP90-ND in the presence of compound 7[3]. d). The mapping of conformation changes due to the ligand derived from HSQC spectrum.

Reference:

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Poster 75

PI3King Apart a Protein Protein Interaction: A Peptide Approach

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Phosphatidylinositol-4,5-bisphosphate 3-kinases (PI3Ks) are a main regulator of cell growth, metabolism and survival, and hyperactivation of these pathways plays a role in many cancers. The PI3K enzymes function at the plasma membrane transducing cell surface receptor activation into internal cell signalling pathways. The PI3Kγ isoform is stimulated on binding to G-protein βγ subunits released upon G-protein coupled receptor (GPCR) activation.[1]

This project aims to target the protein-protein interaction between PI3Kγ and Gβγ as an opportunity for isoform selective PI3K inhibition. Previous work looking at the binding interaction between PI3Kγ and Gβγ has identified a crucial binding motif on one face of PI3Kγ.[2] Synthesis of a library of 10-24 residue peptides derived from PI3Kγ has been completed. A range of stapled peptides has also been explored to improve the peptide binding and stability. The inhibitory activity of these peptides has been evaluated in the lipid kinase biochemical assay. Circular dichroism and molecular modelling have been used to aid prediction of the binding mode. These results, together with the information from a 15 residue peptide bound to Gβγ (Figure 1) will aid the design of an inhibitor.[3] These tools will be used to investigate Gβγ-PI3K pathway activation in cancer cells.

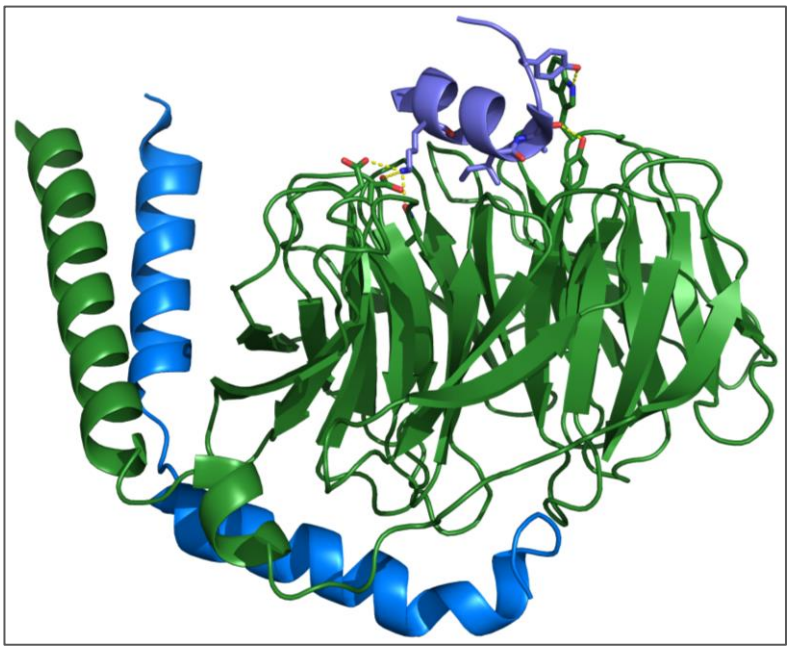

Figure 1. Crystal structure of 15 residue peptide inhibitor (purple) bound to Gβγ (green/blue) (PDB code: 1XHM).[3]

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Poster 76

Conjugation of ruthenium complexes to magnetite nanoparticles for drug delivery

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Since cisplatin's approval in 1978, its anticancer capabilities have opened up the field to other metals such as ruthenium-based complexes as anticancer drugs. Although cisplatin is very effective, it causes a number of side effects due to its non-selective binding nature and also affects normal (non-cancerous) cells.[1] Thus, the search to find new anticancer delivery mechanisms is equally as important as finding new anticancer drugs.

The enhanced permeability and retention effect can be exploited to improve the accumulation of anticancer agents in tumours by loading nanoparticles with anticancer compounds.[2] In this project, ruthenium compounds were developed that contain ligands with different motifs that are able to bind to magnetite nanoparticles (Fe_3O_4) as a potential anticancer drug delivery system (Figure 1). The functionalised nanoparticles were characterised by techniques such as inductively coupled plasma mass spectrometry, transmission electron microscopy and infrared spectroscopy to determine the binding efficacy to the nanoparticles and to determine their morphology.

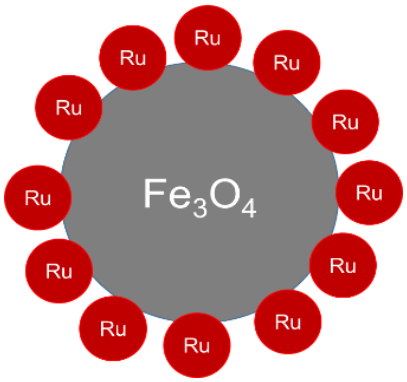

Figure 1. Magnetite nanoparticles surface functionalisation with Ruthenium complexes

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Poster 77

Use of Inorganic Polymers as a Delivery Vehicle for Bioinorganic Anti-Cancer Drugs

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Despite having good cytotoxicity in cancer cells, many new anti-cancer agents are abandoned during development stages because of poor solubility. In recent years, researchers have developed a drug delivery system in which the anti-cancer agents are attached to a support, such as a polymer, which helps to deliver the drug to the tumour site and accumulate in the tissue. This effect is known as enhanced permeability and retention (EPR).[1]

The aim of the project is to attach ferrocifen complexes to an inorganic polymer, poly(phosphazene). Ferrocifen complexes are reported to have excellent cytotoxicity in various cancer cell lines.[2] But, due to poor water solubility, they have failed to qualify for clinical trials. Poly(phosphazene) has been successfully employed as the delivery vehicle for other drugs due to its synthetic versatility as well as its decomposition into non-toxic by-products.[3] Linkers with different lengths and functional groups will be investigated to study the steric effect between the drug and the polymer as well as the stability of the drug delivery system in more acidic and hypoxemic conditions. Different side groups on poly(phosphazene) will also be investigated to optimise the water solubility of the system.

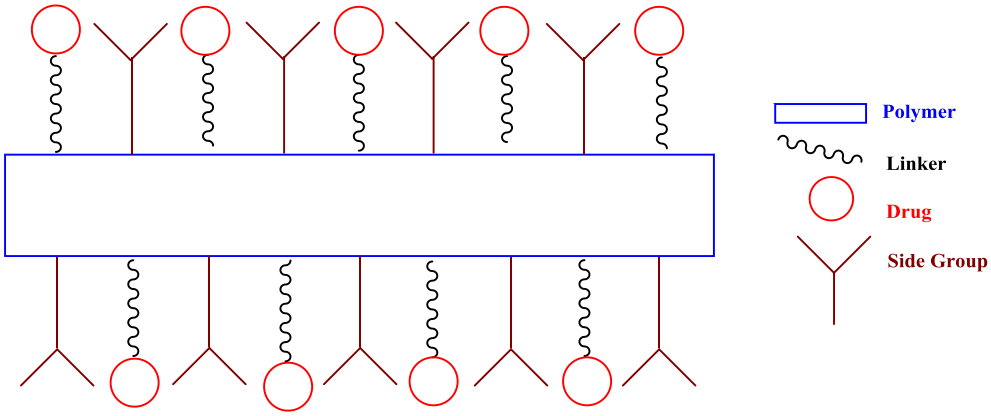

Figure 1. The overview of the drug delivery system

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