Department profile: Chemistry at Trinity College Dublin

The department of chemistry at Trinity College Dublin can trace its origins back to the appointment of Dr. Robert Griffith, a medical graduate of the University, as lecturer of chemistry in 1711. The Department has a rich history, predating one of the earliest chemical milestones: Dalton's 'Law of Multiple Proportions', by over 90 years, and was in its bicentennial year at the time of Rutherford's gold foil experiments. From Griffith's initial appointment, the Department has expanded to a current staff of 39 (21 academic, 15 technical and 3 administrative). The academic staff has quite a young profile, with 67% of appointments dating from 1993.

The Department main building at the east end of the campus dates from 1887 and houses 15 academic staff, with the remainder being located in the nearby Sami Nasr Institute for Advanced Materials (SNIAM); a 6,158m^2 building jointly funded by private donations from individuals, including graduate Sami Nasr, INTEL Ireland Ltd. and the Higher Education Authority under its skills shortage Programme for Research in Third-level Institutions (PRTLI). Further departmental expansion is set to continue in the near future with the construction on campus of two new multi-departmental institutions in which chemistry will play an central role: the SFI-funded CRANN (Centre for Research on Adaptive Nanostructures and Nanodevices) and PRTLI-supported ITAC (Information Technology and Advanced Computing) centres. At present 6 members of staff are also involved of the UCD-led CSCB (the Centre for Synthesis and Chemical Biology).

The Department has two major missions: firstly to maintain the highest standards of undergraduate and graduate education and to develop and evolve such training, and secondly to contribute to the development of the chemical sciences through the pursuit of research excellence.

Teaching

The commitment of the Department to keeping apace with an ever-expanding field has been reflected in the range of courses offered to its students. The 4-year **undergraduate honours course (moderatorship)** provides a broad foundation in the core disciplines of organic, inorganic and physical chemistry. The course places a strong emphasis on experimental technique, and incorporates a three-month research project in final year. Each year a significant proportion of final year students avail of the opportunity to carry out these projects in collaborating institutions abroad. Currently all of the Department's teaching laboratories are newly constructed, and are furnished with State-of-the-art facilities and spectroscopic equipment. The largest of these is the Cocker laboratory, situated in the Hamilton building behind the Chemistry Department.

In recognition of the increasing significance of computation in all branches of chemistry, a moderatorship in **computational chemistry** was instituted in 1997. This course is taught in conjunction with the Physics Department for the first two years, after which the student chooses to study either computational chemistry or physics.

The boundary between chemistry and biology is becoming progressively less distinct, resulting in a growing demand for chemistry graduates able to interact and collaborate with biologists. The moderatorship in **medicinal chemistry** trains students to work effectively at the interface between chemistry and chemical biology. The first two years provide a solid chemical background, after which time students specialise in synthetic chemistry and subjects related to the intricate science of drug design. Graduates from this course, the first of which emerged in 2003, are ideally suited for employment in the pharmaceutical industry; a sector in which Ireland is a world leader.

Recent years have also witnessed an acute demand for new materials to serve as (*inter alia*) platforms upon which to build faster, smaller and more efficient electronic devices. The relatively young science of nanotechnology has an important role to play in this area and has been identified as a high-potential field for investment by the government.[1] In response to a projected skills shortage in this area, the Department has introduced moderatorship in **the physics and chemistry of advanced materials**. Graduates are specialists in the design and synthesis of modern materials for electronic, optoelectronic and related applications.

In addition to training the next generation of chemists, the Department teaches chemistry to undergraduates from the Medical, Health Sciences and Engineering faculties, and takes a particular interest in the needs of students who have not previously studied chemistry. A part of the TCD Broad Curriculum exercise, the Department offers students from across the college the opportunity to learn about the contemporary relevance of chemistry through small-group research projects on topical issues, the completion of which involves a presentation to an audience consisting of students and members of staff. The standard of these presentations is uniformly excellent, and the best four presentations are invited to a grand final to compete for the Broad Curriculum trophy.

Through constant review of its diverse degree portfolio, the Department strives to produce highly skilled graduates (numbering 42 in 2004) trained in the techniques necessary to meet the current needs of both the dynamic Irish chemical industry and the rapidly developing, increasingly competitive research environment in the country.

Figure 1. (*left to right*) Chemistry main building, the Cocker laboratory, the SNIAM building, Prof. J. Apjohn, apjohnite, Prof. J. E. Reynolds.

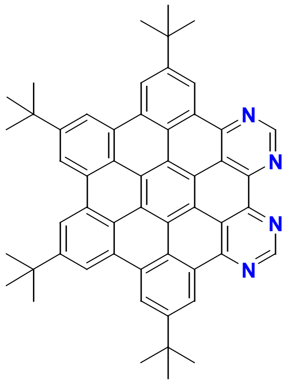
Research

The Department has a long tradition of research excellence.[2] The first professor of chemistry to be primarily concerned with experimental science (as opposed to medicine) was Prof. James Apjohn (1850-1875), whose interests ranged from chemistry and physics to mineralogy, and who gave his name to the mineral apjohnite $[MnAl_2(SO_4)_4.22(H_2O)]$ (Figure 1). Apjohn was succeeded by Prof. James Emerson Reynolds, renowned for the first synthesis of thiourea in 1869.[3] A major reorganisation of the Department began under **Prof. Wesley Cocker** in 1946 resulting in a greater emphasis being placed on research, in line with the trends in other institutions around the world at the time.

The current head of department **Prof. John Corish**, and his predecessor **Prof. John Kelly**, have overseen a further period of transition, with the appointment of 14 new members of staff, including SFI fellows **Prof. John Boland** (formerly at The University of North Carolina at Chapel Hill) and **Prof. Mathias Senge** (formerly of the University of Postdam), the construction of both the SNIAM building and the Cocker Laboratory together with the renovation of existing departmental research facilities (currently in progress). Consequently the Department has found itself in a strong position to compete for funding from governmental, EU and other grant authorities and research income has increased dramatically in recent years.

While the research interests of the Department are wide ranging, spanning diverse fields such as chemical biology and organic synthesis/catalysis, polymers/nanotechnology, inorganic and supramolecular chemistry, chemistry theory and computation, electrochemistry and analytical chemistry/sensor devices, in general the thrust of the departmental research endeavour mirrors that of its teaching; with emphasis placed on molecular synthesis, computational chemistry and the development of innovative advanced (nano)materials. The postgraduate population of the Department is expanding rapidly, and presently numbers *ca*. 70 students studying for Ph.D. and Masters degrees. This is set to grow further as the Department (in collaboration with the Biochemistry Department) develops a new taught masters degree course in the Chemical and Biological application of Spectroscopy, Instrumentation and Modelling (CABSIM). A short summary of a selection of research that has been recently carried out in the department is presented below.

Dr. Sylvia Draper and her research team have prepared the first member (Figure 2) of an amazing family of molecules that they have called nitrogen heterosuperbenzenes: it contains 13 fused rings and resembles a nitrogen-doped fragment of graphite. The team expect that this molecule will find use in a range of opto-electronic applications because it is stable to heat, soluble and fluoresces very intensely. This compound can be justifiably called a ‘traffic-light’ molecule, because under UV light it fluoresces with different colours depending on the solvent in which it has been dissolved.[4]



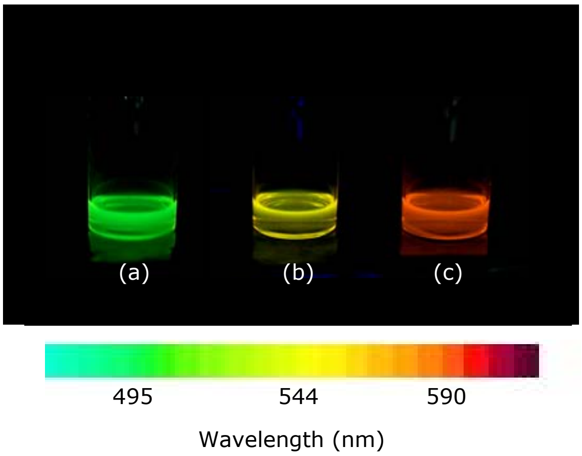


Figure 2. The first nitrogen heterosuperbenzene (left) and its appearance under UV light in (a) toluene, (b) chloroform and (c) methanol solutions.

PaTrin-2 (Figure 3) is a drug with potential use in cancer chemotherapy which has been prepared by the group headed by **Prof. Brian McMurry** and **Dr. Stanley McElhinney**. So named because of the collaboration in its development between the Trinity group with Dr. Geoff Margison of the Paterson Institute in Manchester, it is currently being tested in Phase II clinical trials in the U. K., Austrialia and the U. S. A. PaTrin-2 is not in itself an anti-cancer drug, but is designed to inhibit the enzyme O^6-alkylguanine-DNA-alkyltransferase (ATase); a so-called 'suicide protein' which repairs damage to the cell's DNA caused by chemotherapeutic alkylating agents. Patrin-2 is administered along with an alkylating drug such as temozolomide.[5]

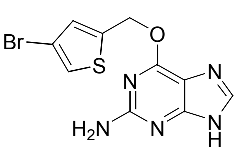
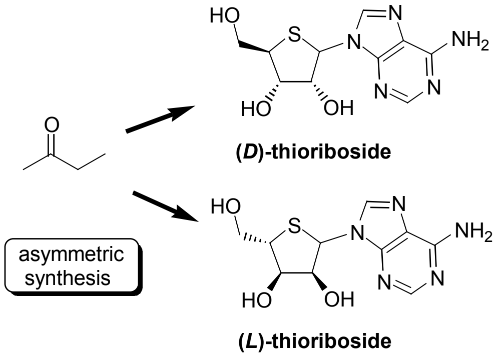


Figure 3. PaTrin-2: A potential chemotherapy drug in phase II clinical trials.

Dr. Mike Southern and his research group are preparing enantiopure heterosugars (Figure 4) from non-carbohydrate sources, in which the endocyclic oxygen atom is replaced with a heteroatom (*e.g.* sulfur, selenium or tellurium). Materials such as these (thiosugars in particular) are known to exhibit both anti-viral and anti-bacterial activity. The novel synthetic route to these compounds does not rely on the chiral pool, allowing the preparation of diverse array of natural and unnatural stereoisomeric analogues. The (*L)*-heterosugars are generally not recognised by mammalian enzymes but are compatible with, and can therefore disrupt, virus encoded- or bacterial enzymes, thus minimising side-effects in the patient. Potential applications in cancer chemotherapy are also being investigated.



Thionucleosides

- (*L*)-isomer generally not recognised by mamailian enzymes
- often recognised by bacterial and viral enzymes (including reverse transcriptases)
- available as either antipode via a novel concise non-carbohydrate-based route
- **hold much promise as selective, non-toxic anti-infective agents**

Figure 4. Thioribosides: Prospective anti-infective agents

Dr. Dónall Mac Dónaill is engaged in trying to answer fundamental questions such as why the four DNA nucleotide bases (A, G, C and T) were selected as the genetic alphabet in preference to other, at first seemingly equally probable alternatives.[6] Dr. Mac Dónaill has developed an entirely new method of evaluating the optimal size and composition of the DNA alphabet by realising that DNA replication, as an information transfer process, must be subject to the constraints of informatics (a science most often associated with digital electronic data transmission). By observing that the nucleotide recognition features can be expressed as a 4-bit binary vector (Figure 5) where a lone-pair = 0, H-bond donor = 1 and a fourth digit is determined by whether the base is a purine (0) or a pyrimidine (1), using established principles of informatics he has shown for the first time that the natural alphabet optimally balances the opposing constraints of information density and replication error-avoidance. Possible alternative alphabets either incorporate an unstable nucleotide or violate the rules of informatics.

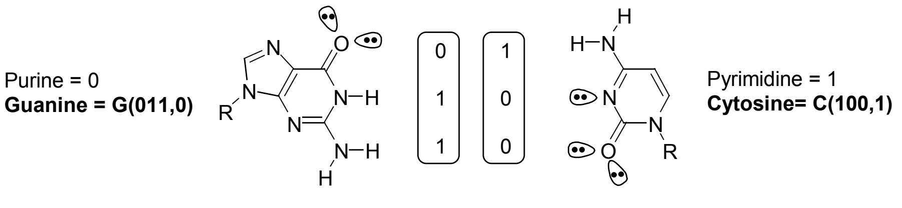


Figure 5. Guanine and Cytosine encoded as 4-bit binary vectors

Dr. Yuri Gun'ko and his group, in cooperation with colleagues in the Physics Department have developed a creative new method for the fortification of polymers using organometallically functionalised carbon nanotubes. Nanotubes are sheets of graphite folded back on each other to form cylinders of incredible strength. The technique utilises an addition reaction between carbon nanotubes and *n*-butyllithium to generate a nucleophilic polyanionic intermediate, which then undergoes a substitution reaction with chlorinated polypropylene (CPP), thereby covalently binding the nanotubes to the polymer. When as little as 0.6 vol % (or 1 wt %) of this novel nanohybrid material is incorporated into a thin film of chlorinated polypropylene itself, the new polymer is three times more elastic, while tensile strength and toughness increase by factors of 3.8 and 4.0 respectively. Conservative extrapolation of these results show that increases in strength by a factor of 10-20 should be possible for any polymer if the nanotube content can be increased to 10 vol %. This approach can be used to reinforce most known plastics, potentially leading to new ultra-strong polymer composite materials.[7]

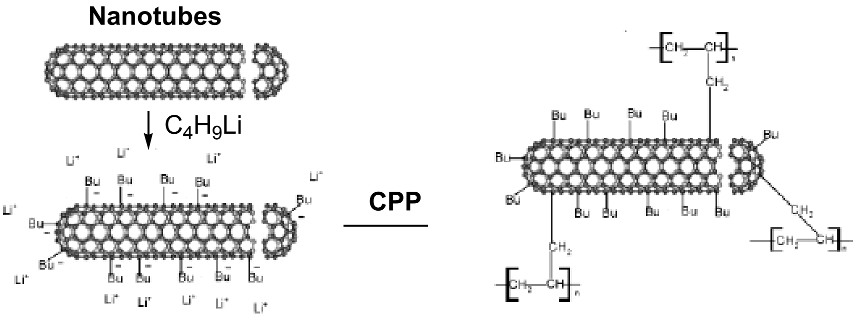


Figure 6. Synthesis of a novel nanotube-fortified polymer.

Dr. Thorri Gunnlaugsson and his team have designed a series of sensors which exploit the quenching of lanthanide luminescence to detect cations. The sensors consist of an 'antenna' which is excited photometrically, causing energy transfer to the lanthanide ion (lumophore) and subsequent long-lived emission in the 500-700nm range which is easily detectable. Binding of the antenna to a metal ion or proton analyte arrests the energy transfer mechanism resulting in loss of emission and detection of the cation. Several of these systems have been shown to be very analyte-selective, for example the complex shown in Figure 7 (*left*) serves as a physiological pH responsive–sensor as well as a selective Cu(II) ion sensor. The same group have also recently designed a lanthanide-free highly selective 'naked-eye' Cu(II) ion sensor (Figure 7, *right*), with potential applications in the diagnosis and treatment of Menkes disease; an often fatal condition in young boys resulting from the irregular metabolism of copper.[8]

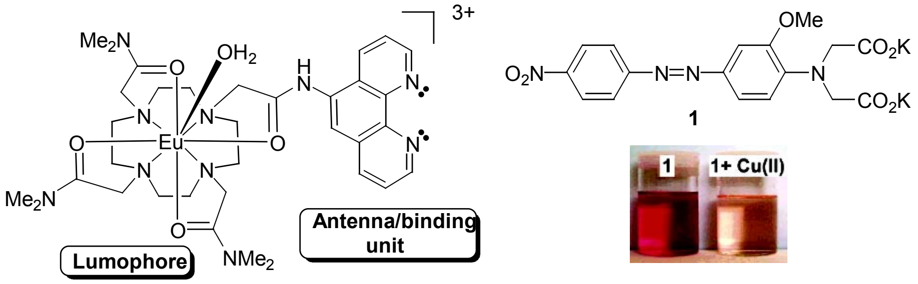


Figure 7. pH-responsive (*left*) and 'naked-eye' Cu(II) ion (*right*) sensors.

Prof. John Kelly and his group have prepared oligodeoxynucleotide-linker-Ru(phen)$_3$ conjugates capable of inflicting photooxidative damage predominantly at one guanine base in a single strand of target DNA present in a gene detected in 95% of patients suffering from chronic myeloid leukaemia. The conjugate consists of an oligonucleotide (the composition of which is complimentary to that of the object DNA, thus ensuring selective binding to the target) attached *via* a linker to a photoactive ruthenium complex. On irradiation of the conjugate-target complex with UV-visible light, the ruthenium complex brings about photooxidation of the nearby guanine-21 residue (Figure 8), leaving the target DNA strand vulnerable to alkali-mediated cleavage at this position.[9] This methodology holds great promise as a novel hybrid of both antisense- and photodynamic therapy in which both selective binding and substrate damage are possible, with potential applications in treatment of cancers and a diverse array of other diseases.

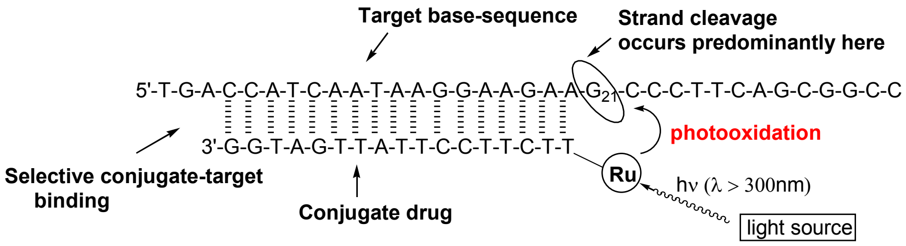


Figure 8. Novel oligonucleotide-ruthenium complex conjugates for antisense therapy

Prof. Mathias O. Senge and coworkers have developed the first general method for the synthesis of unsymmetrically substituted porphyrins (Figure 9, *left*). Using S$_N$Ar reactions various numbers, types and regiochemical arrangements of substituents can now be introduced into the porphyrin system. Porphyrins are ubiquitous biological cofactors, they play a crucial role in many diseases, they are important industrial pigments, and they have significant potential as photosensitisers in biotechnology and as photoactive drugs in medicine. Two examples for ongoing work at the interface of chemistry and biology are the construction of nonplanar porphyrins (Figure 9, *middle*) as models for enzyme function, and the utilisation of unsymmetrically substituted "ABCD-porphyrins" (Figure 9, *right*) as photosensitisers for photodynamic cancer therapy and diagnosis.[10]

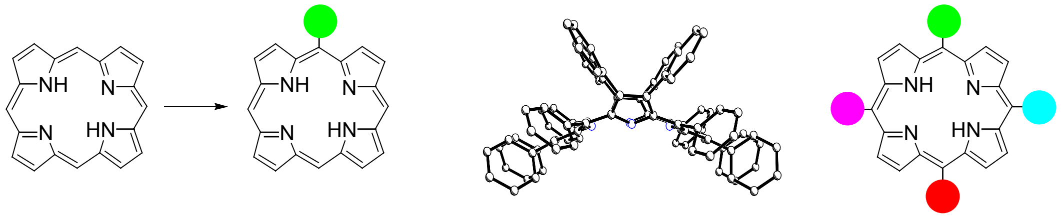


Figure 9. Molecules with exciting properties and great biotechnological and medicinal relevance.

While retaining many traditions from its long history, the chemistry Department at TCD has evolved over the last three centuries years to into a modern, forward-thinking institution with a vibrant research community and a commitment to producing graduates possessing both a broad chemical knowledge and expertise in the more specialised fields such as computation, materials chemistry and drug-design; topics which look certain to be crucial to the development of the Irish chemical industry and the economy as a whole.

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