ScotCHEM 2014

Session 1 — Chair: Prof. Martin Paterson

10:20	Opening Remarks (Head of the Institute of Chemical Sciences)	Prof. Stuart Macgregor, *Heriot-Watt University*	
10:30	**PLENARY TALK:** *Mapping molecular currents: simple pictures of aromaticity and molecular conduction*	Prof. Patrick Fowler, *University of Sheffield*	O1
11:20	*Computational modelling of organic semiconductors for optoelectronics*	Prof. Ian Galbraith, *Heriot-Watt University*	O2
11:50	*Helical nanosystems*	Dr Ben Hourahine, *University of Strathclyde*	O3
12:20	Lunch	Earl Mountbatten 1.83	

Session 2 — Chair: Dr Carole Morrison

13:20	*Identifying trapped electronic holes at the TiO_2 water interface*	Dr Jun Cheng, *University of Aberdeen*	O4
13:50	*Excited states and potential curves using Monte Carlo configuration interaction*	Dr Jeremy Coe, *Heriot-Watt University*	O5
14:10	*Impact of ligand binding on the N-terminal MDM2 lid dynamics explored by accelerated molecular dynamics and umbrella sampling*	Dr Juan A. Bueren-Calabuig, *University of Edinburgh*	O6
14:30	*Active site structure from docking and dynamics: the non-heme Fe halogenase SyrB2*	Mr Graham Rugg, *University of Glasgow*	O7
14:50	Tea/Coffee	Postgraduate centre	

Session 3 — Chair: Dr Hans Martin Senn

15:20	*DFT study of a rhodium(I) σ-alkane complex: mechanism and bonding*	Dr Tobias Krämer, *Heriot-Watt University*	O8
15:40	*Uncovering the mechanism of MMA production at a palladium catalyst - accounting for selectivity and reaction conditions*	Mr Luke Crawford, *University of St. Andrews*	O9
16:00	*ARCHER: the UK national supercomputing service*	Dr Andrew Turner, *EPCC*	O10
16:10	Flash Presentations		

F1	**Georgios Gerogiokas**	*Biomolecular hydration thermodynamics via grid cell theory aids prediction of ligand-protein binding affinities*
F2	**Nuno Almeida**	*Challenging systems for quantum chemistry: intermolecular aggregates and inorganic excited states*
F3	**Greg Anderson**	Organic super-electron-donors: initiators in transition metal-free haloarene-arene coupling
F4	**Divya Sharma**	*Computational analysis of benzene interaction with crystalline ice surfaces: ground and excited state investigations*
F5	**Leo Holroyd**	*Mutagenic mispairing of 5-bromouracil*
F6	**Peter Repiščák**	*Multi-scale computational modelling of complex molecular systems: from CuNO to polyfluorenes*

Mapping molecular currents: simple pictures of aromaticity and molecular conduction

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Ring currents are famously used to diagnose aromaticity. This talk will deal with the ab initio computation and the interpretation of induced currents, showing how the size, direction and distribution of current in a wide variety of systems can be understood with simple ideas based on familar concepts of orbital energy, symmetry and nodal character. The MO picture will be compared with the recent revived empirical conjugated-circuit models, which have their own insights to offer, especially about overall topography of current patterns.

Computational Modelling of Organic Semiconductors for Optoelectronics

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In films of organic semiconducting materials, the ultrafast photophysics is dominated by excited-state processes, such as inter-molecular exciton transfer and annihilation. For improving the efficiency of devices such as OLEDS and organic photovoltaic cells, knowledge about these microscopic processes is of particular importance. Here we present an experimental and theoretical study of excited-state processes in such films. The materials chosen for this study are oligo- and poly-fluorenes, which are of particular interest as they are efficient emitters, used e.g., in OLEDS.

The exciton dynamics is inferred experimentally from fluorescene anisotropy measurements: following a resonant excitation by an ultra-short linearly polarised light pulse, a sub-picosecond decay of the emitted fluorescence polarisation anisotropy is observed. We show that an averaged, macroscopic estimate, based on Forster inter-molecular transfer theory, leads to predictions of exciton transfer and depolarisation around 20 times slower than observed experimentally.

We therefore developed a microscopic model of the exciton dynamics in the film to account properly for both the physical and spectral morphologies of the film, in order to provide a more refined, and more realistic, estimate of the exciton diffusion timescale. Our model consists of a set of rate-equations describing the exciton density of each chromophore, and uses input parameters obtained by quantum chemistry and from the measured spectra. The fluorescence anisotropy decay we predict agrees with the experimental observations very well. In addition, we obtain good predictions of exciton diffusion lengths. This demonstrates that when the microscopic film properties are well accounted for, dipole mediated exciton hopping is sufficient to fully explain the observed sub-picosecond dynamics.

Helical nanosystems

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Nano-wires of semiconducting material often contain threading dislocations, which modify their structural and electronic properties. While the atomistic and electronic structure of edge dislocations in these columns have been theoretically studied by several groups, investigations into screw dislocations are much rarer. This is largely due to to the additional complications of the resulting helical geometry of such structures [1]. The conventional translational repeat unit cell of such twisted geometries can easily contain millions of atoms, however the fundamental repeat unit of the structure is far smaller.

In order to investigate the electronic structure and properties of such helical structure with realistic diameters, we have recently extended the density-functional based tight binding method to self-consistently treat these geometries [2]. This technique treats systems self-consistently and also includes contributions for dispersion forces, but can additionally be applied to open shell or spin-orbit driven systems and strongly correlated materials. This enables the use of "objective" boundary conditions to study the energetics and electronic structure of twisted nano-columns, chiral wires, helical nanotubes and helical molecules, and examples of these systems will be given to illustrate the approach.

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Identifying trapped electronic holes at the TiO_2 water interface

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Trapping of photo-generated holes near or at the surface is a crucial step in photocatalytic reactions on TiO_2, e.g. the oxidation of water and organic pollutants. The identity of the trapped holes is still under debate, and some experimental interpretations even appear conflicting. In this talk, I will present our recent calculations of the trapped holes at aqueous rutile TiO_2(110) surface using ab initio molecular dynamics based on the hybrid functional HSE06. We found that the reactive surface trapped holes as the $OH^{\bullet}$ on five-coordinated terminal Ti and its deprotonated $O^{\bullet-}$. I will also discuss the alignment of both the vertical and adiabatic electronic energy levels of the trapped hole states. The vertical levels are what electronic spectroscopies (e.g. photoemission and transition adsorption) measure. The thermodynamic stabilities (or reversely activities) of the holes are however determined by the adiabatic levels (i.e. redox free energies). The confusions between these two often lead to the conflicting interpretations. Their differences are reorganization energies, which can be on the order of 1-2 eV and are important for the electron transfer kinetics according to Marcus theory. We also observe an asymmetry in reorganization energies owing to the pinning of the valence band of TiO_2. This has important implications for the understanding of the heterogeneous electron transfer kinetics driving photo-oxidation.

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Excited states and potential curves using Monte Carlo configuration interaction

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A wavefunction that can capture much of the full configuration interaction result but using only a very small fraction of the configurations may be iteratively constructed using the stochastic procedure of Monte Carlo configuration interaction (MCCI) [1]. We have incorporated state-averaging into MCCI which we have then applied to excited-state potential energy curves, including conical intersections, and to the computation of vertical excitations in small organic molecules [2]. We next consider if the use of MCCI approximate natural orbitals and second-order perturbation (MCCIPT2) [3] can improve the accuracy of vertical excitation energies. We also discuss natural transition geminals [4] as an approach to qualitatively characterise an excited state modelled with configuration interaction when double orbital excitations from the ground state are important.

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Impact of ligand binding on the N-terminal MDM2 lid dynamics explored by accelerated Molecular Dynamics and Umbrella Sampling simulations

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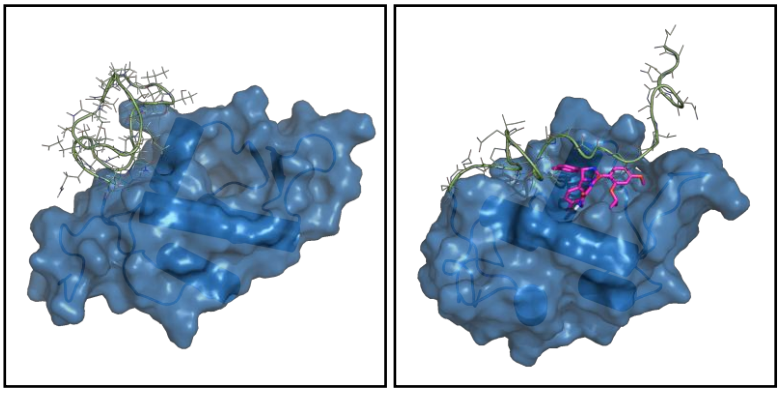
The oncoprotein MDM2 is a negative regulator of the tumor suppressor protein p53. The disruption of the p53-MDM2 complex induced by ligand binding constitutes a very promising strategy in cancer research.[1] The N-terminal domain of MDM2 is partially folded (residues 25-119), whereas the first 24 amino acids form a disordered "lid" region in the apo state that competes for the p53 binding site via a pseudo-substrate mechanism.[2] Several structural, biochemical and theoretical experiments have shown that the lid can adopt two possible conformations: one 'open' conformation in which p53 is able to bind MDM2, and one 'closed' that occludes the p53 binding site. In addition, the lid can also undergo a disorder-to-order transition upon binding of small molecules to MDM2.[3] However, the exchange between the different lid conformations take place on a vey slow time scale (>10-ms)[4] which is often outside the reach of canonical MD simulations. To achieve sufficient sampling of lid conformations with reasonable computing resources, we have combined two different enhanced sampling techniques: accelerated molecular dynamics (aMD) and umbrella sampling (US). With the combined aMD/US protocol we have completed extensive simulations of MDM2 with a complete lid (residues 1-119) in the absence and presence of several ligands of pharmaceutical relevance. Our studies provide new insights into the interplay between MDM2 lid dynamics and ligand interactions, and may contribute to the design of new and more effective p53-MDM2 inhibitors.



MDM2 structures showing the **N-terminal lid domain** (green) conformations in the **open state** (left, apo-MDM2) and in the **closed state** (right, in the presence of **Nutlin 3a**)

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Active Site Structure from Docking and Dynamics: the Non-Heme Fe Halogenase SyrB2

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The non-heme Fe halogenase SyrB2 chlorinates the methyl group of the amino acid l-threonine during the biosynthesis of syringomycin E. Although other chlorinase enzymes have been known for some time, SyrB2 was the first member of the family of Fe(II) 2-oxoglutarate dependent halogenases to be discovered. These enzymes employ a radical rebound reaction involving a high-spin Fe(IV) intermediate. Similar mechanisms are employed by a diverse family of enzymes for a range of reactions, from hydroxylation to cyclisation. Despite the exciting implications to synthetic chemistry of the chlorination of an unactivated methyl group, and increasingly successful attempts at biomimicry, the mechanism is still not well understood, specifically the structure of the Fe(IV)=O active site species, and why, when presented with several non-native substrates, SyrB2 is willing to hydroxylate rather than chlorinate them. This talk describes our study of protein-ligand interactions through docking and molecular dynamics, as we attempt to elucidate the influence of substrate placement by comparison of docked and solvated structures for three ligands in complex with SyrB2.

DFT Study of a Rhodium(I) σ-Alkane Complex: Mechanism and Bonding

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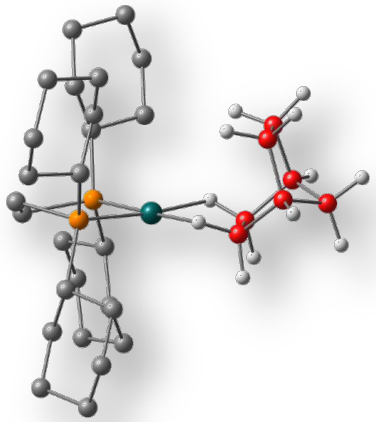
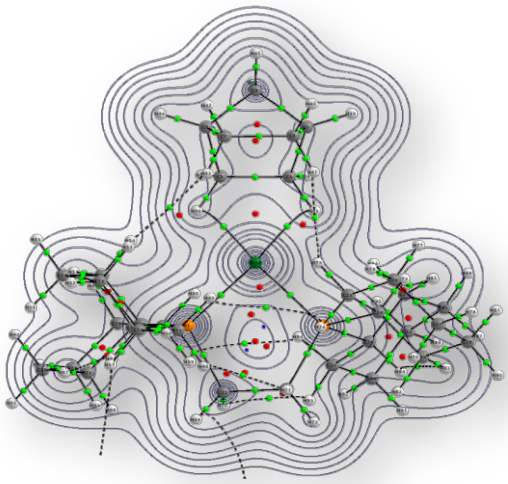
Transition metal σ-alkane complexes, in which an alkane coordinates directly to the metal centre, are key intermediates in catalytic C–H activation processes.[1] Insight into the electronic structure of these species is fundamental for the understanding of the C–H activation process, and ultimately facilitates the design of improved catalysts. Adopting a solid-gas synthetic route, the Weller group recently reported the first example of a crystallographically characterised transition metal alkane σ-complex, $[Rh(dibpe)(norbornane)]^+$ (dibpe = $^{i}Bu_2PCH_2CH_2P^{i}Bu_2$).[2] Subsequently, the synthesis and isolation of a related - and particularly stable - σ-complex, $[Rh(dcype)(norbornane)]^+$ (dcype = $Cy_2PCH_2CH_2PCy_2$) has been achieved.



Density functional calculations (DFT) were employed parallel to experiment to confirm the metal-alkane structure in $[Rh(dcype)(norbornane)]^+$. Quantitative insight into the [Rh]···HC interaction in this complex was gained through combined atoms-in-molecules (AIM) and natural bond orbital (NBO) analyses of its electronic structure. Bond metric data are indicative of a weakening of the coordinated C–H bonds and, in combination with the presence of bond critical points along the Rh···H bond paths, are clear evidence for a σ-interaction. NBO highlights that the major component of the [Rh]···HC interaction is derived from donation of electron density from the C–H σ–orbital to the metal centre, complemented by π-back donation involving Rh-centred orbitals and the C–H σ*–orbital. Further DFT calculations mapped out the potential energy surface of the mechanism of the solid-gas hydrogenation reaction yielding the NBA products. The computed mechanism accounts for the unusual *endo-endo* selectivity in the product observed at low temperature.



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Uncovering the Mechanism of MMA Production at a Palladium Catalyst – Accounting for Selectivity and Reaction Conditions

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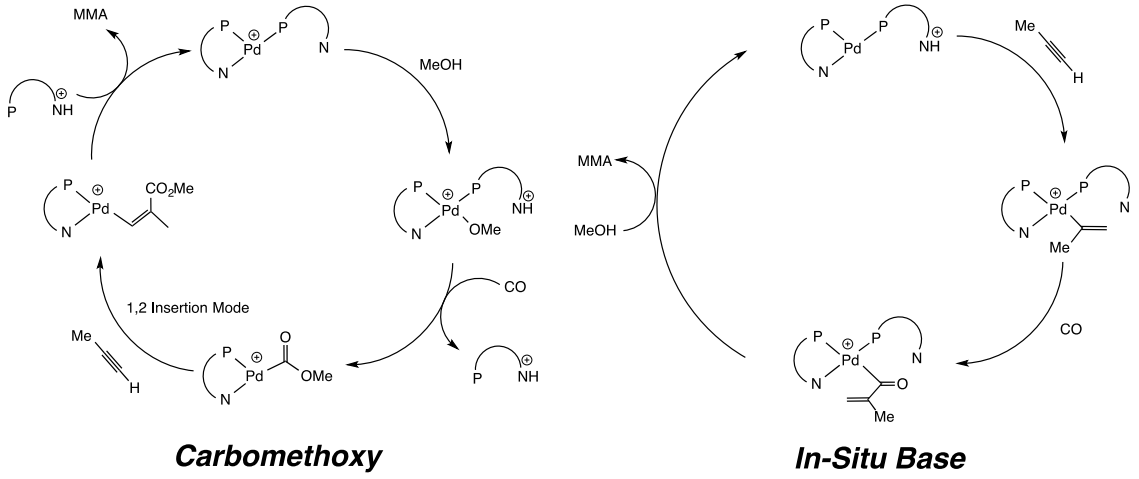
Methyl methacrylate (MMA) is widely used as a precursor for poly(methyl methacrylate) and is itself an important chemical commodity. One commercialized route to the production of MMA involves carbonylation of propyne in methanol using palladium acetate in the presence of 2,6-bis-(biphenyl phosphino) pyridine (2-PyPPh$_2$) under acidic conditions[1]. However, the catalytic cycle followed experimentally is not entirely understood and thus truly rational improvement or design of new catalysts is currently not feasible. Catalytic cycles proposed so far[2,3] have concentrated upon the ability of the P,N ligand to act as both a hemilabile chelate and also a mono-coordinating species – with a potentially basic moiety – at different times in proposed catalytic cycles, two of which are outlined in Scheme 1.



Scheme 1: Two potential routes to MMA incorporating 2-PyPPh$_2$ as a proton messenger.

To be reconciled with experimental observations, the correct mechanism must present surmountable barriers and reproduce the obtained regioselectivity – MMA over methyl crotonate. Furthermore, the mechanism must explain how this regioselectivity depends on substituents at the pyridyl moiety of the ligand[4] and how more acidic conditions would accelerate the reaction[5].

Considering such stipulations we have investigated four different catalytic cycles that could plausibly produce MMA using modern density functional methods. Our methodology involves a robust hybrid functional, semi-empirical dispersion corrections and bulk solvation through a continuum model. Computations at such a level of theory suggest that typical carbomethoxy and hydride routes involving one 2-PyPPh$_2$ ligand in a chelating mode have too high barriers for protonolysis and solvolysis. Processes involving a secondary P,N as a proton relay are much more feasible. We identify one mechanism in particular involving Pd(0) and a P,N "in-situ base" that is consistent with all experimental observations.

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ARCHER: the UK national supercomputing service

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I will give a brief introduction to the UK national supercomputing service: ARCHER, which is housed at the University of Edinburgh and run by EPCC. Computational chemistry codes make up the bulk of usage on the service and I give an overview of the usage patterns of these codes.

Finally, I will also mention mechanisms for getting access to ARCHER for your research.

Biomolecular hydration thermodynamics via grid cell theory aids prediction of ligand-protein binding affinities

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Prediction of binding free energy can aid acceleration of the drug discovery and optimisation process. However, many current predictors do not account for the hydration thermodynamics. A novel, efficient methodology has been developed to quantify water energetics through an analysis of explicit solvent molecular simulations of organic and biomolecular systems. The approach, grid cell theory (GCT), relies on a discretization of the cell theory methodology on a three-dimensional grid to spatially resolve the density, enthalpy and entropy of water molecules in the vicinity of system(s) of interest for qualitative and semi-quantitative analyses [1].

Using GCT we investigate ligand-protein systems by computing numerical estimates of the energetics of desolvation from suitable thermodynamic cycles. This involves simulating protein, ligand and complex structures of your system of interest, in our case of a congeneric series of Hsp90 ligands [2]. The hydration energetics of each state gives a physically intuitive understanding of the water reorganisation cost of binding incurred by the protein and ligand desolvation energies as well as complex solvation energy. These thermodynamic states can be visualised as isosurfaces allowing identification of stable and unstable water sites. These GCT desolvation terms coupled with interaction energies between the protein and ligand can be used to compute a predictive protein-ligand score which should prove useful during ligand optimisation.

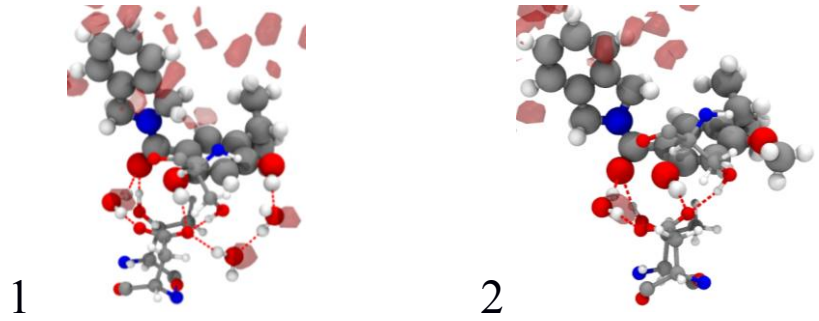

Figure. The spatial resolved grid of the hydration ΔG in the protein-ligand structures are shown as isosurfaces. ASP 93, THR 184, and SER 52 are shown in smaller VDW spheres while the selected ligands, **1 and 2**, are shown in larger VDW spheres. Hydrogen bonds are displayed as red dotted lines while the red isocontours of each hydration grid is generated using an isovalue of -16 kcal mol^{-1} $Å^{-3}$.

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Challenging systems for quantum chemistry: intermolecular aggregates and inorganic excited states

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Supramolecular structures have grown in importance in recent years due to their potential applications as advanced functional materials. The fine-tuning of these structures allows building up higher hierarchical superstructures with very diverse and interesting properties. Theoretical calculations using DFT (Density Functional Theory) investigating the self-assembly of p-{[4,6-Bis(p-carboxybenzoylamino)-1,3,5-triazin-2-ylamino]carbonyl}benzoic acid hydrogel were carried out. A bottom-up approach for this kind of systems is used to characterize the multichromophoric self-assembly of pH dependent gels[1], and detail their responses to light.

A strong π-π interaction is fundamental to keep these structures together as well as strong hydrogen bonding. In biological structures these types of interactions play a major role. A good example is the intercalation of porphyrins with DNA. The structure of d(CGATCG) - CuTMPyP4 could help explain the aspects of electron-transfer processes that occur in DNA. The complex is stabilized by electrostatic interactions between the nitrogen atoms in the porphyrin and the negatively charged phosphate groups. This phenomenon also causes an increase of the specific viscosity in solution of the DNA. A theoretical study using DFT and QM/MM (ONIOM) of this biological system is also presented[2].

Excited states of inorganic systems can be extremely challenging for conventional methods of quantum chemistry, mostly due to strong correlation, degeneracy and near-degeneracy problems, in addition to a large density of states. A benchmark study of the electronic excited states of a range of complexes has been carried out using a range of coupled cluster response methods (CCS, CC2, CCSD and CC3) and time-dependent (TD)-DFT. A range of both all-electron and ECP basis sets are also used. These calculations reveal the effect of systematically improving the treatment of electron correlation. The calculated results are compared with each other and experimental values where available. Finally, several pathological features of popular response methods have been identified that are not apparent in organic systems[3,4].

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Organic Super-Electron-Donors: Initiators in Transition Metal-Free Haloarene-Arene Coupling

S. Zhou, G. M. Anderson, B. Mondal, E. Doni, V. Ironmonger, M. Kranz, T. Tuttle, J. A. Murphy

University of Strathclyde

Within both industrial and academic settings, the coupling of two aryl moieties is a process of significant synthetic value. To achieve such transformations typically requires the use of expensive transition metal catalysts that cannot always be recovered from reaction mixtures. As such, the investigation of biaryl coupling reactions without any requirement for such catalysts has been of key interest amongst chemists.

Outlined in this work is the ability of a number of reagents, termed incorrectly as "catalysts" or "ligands" within the literature, to form organic super electron donors *in situ* following reaction with a strong base. These electron donors are capable of reducing an aryl iodide to its radical anion, which can then dissociate to the corresponding aryl radical following the loss of iodide. Provided that there is sufficient base present, a cyclic radical pathway leads to the formation of biaryl products.

Support for experimental observations has been obtained through the application of Density Functional Theory to probe both the energetics and feasibility of proposed mechanistic pathways. Results from these studies agree with the requirement for high temperature reaction conditions, and suggest such conditions are required in order to drive the donor-forming reactions forward.

Computational analysis of benzene interaction with crystalline ice surfaces: Ground and excited state investigations

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Infrared observations on these icy mantles have shown water as the most abundant molecule in icy grain mantles. Polycyclic aromatic hydrocarbons (PAHs) are a particularly important class of aromatic molecule, which may account for up to 20 % of the galactic carbon and are likely to exist in the presence of water ice as either a part of the carbonaceous component of the dust grain itself or as a component of icy mantles. Benzene may be thought of as a prototypical PAH compound and is amongst the list of known interstellar molecules and water ice is a good representation of icy mantles on grains. Therefore, the computational study of the ground and excited states of the complexes of the benzene (Bz) with ice surfaces is of astrophysical relevance.

In our work, we focused on investigating ground state structures and energetics of complexes of Bz with crystalline ice surface. Two crystalline ice surfaces consisting of four binding sites each and respective Bz-ice complexes are optimized with ONIOM QM/MM methodology. Four binding sites consists of 3 d-H; 2 d-H 1 d-O; 1d-O 2 d-H; 3 d-O, where d-H and d-O denotes dangling hydrogen and dangling oxygen, respectively. We used DFT functional MO62X with 6-31++G** basis set as high level method for QM layer and AMOEBA force field for MM layer. Binding energies of Bz with ice surfaces are found to be dependent on the nature of binding sites that influence the energetics, with structure consisting of binding site (2 d-H 1 d-O atom) is of higher binding energy ≈ 10 kcal/mole. TD-DFT calculations are performed to investigate excited states of all eight ONIOM optimized ground state geometries of Bz- ice complexes using M062X functional and 6-31++G(d,p) basis set. Our results show that lowest singlet $\pi \rightarrow \pi^*$ electronic transition of benzene is red shifted under the influence of water cluster. Charge transfer (CT) states and diffuse Rydberg-type states are also found to play an important role in such complex systems.

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Mutagenic mispairing of 5-bromouracil

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5-Bromouracil (BrU), a structural analogue of thymine, is a potent experimental mutagen. It exerts its mutagenic effect by mispairing with guanine instead of adenine in DNA, causing both AT→GC and GC→AT point transitions. This is analogous to the thymine-guanine mispairing which was proposed by Watson & Crick as the cause of spontaneous mutations involving the natural bases.

Spontaneous mispairs are generally assumed to involve minor tautomers of one base or the other – the so-called "rare tautomer hypothesis" (Figure 1). It follows that the enhanced mutagenicity of base analogues may be due to their greater propensity for tautomerisation.[1] However, experimental evidence for this hypothesis in relation to BrU is hard to come by.

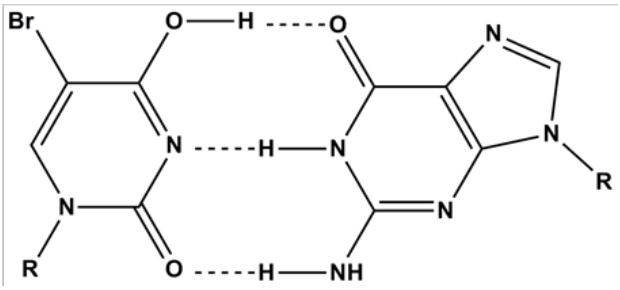

Figure 1 – Potentially mutagenic mispair between the minor (enol) tautomer of 5-bromouracil (left) and the major tautomer of guanine (right). Despite the mismatch the bases are in Watson-Crick geometry.

The poster presents computational research into several lines of enquiry – to what extent does solvation in water nanodroplets influence the tautomeric constant of BrU, as assessed by various functionals; what is the role of water in the dynamical tautomerisation process (i.e. proton transfer), as modelled by CPMD; and can the abundance of BrU-G mispairing be better explained by enhanced intrastrand base stacking of BrU, as measured by double-hybrid functionals and df-LCCSD(T).[2]

The results broadly support the rare tautomer hypothesis.

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Multi-scale computational modelling of complex molecular systems: From CuNO to Polyfluorenes

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Theoretical investigation of complex systems of different system size often requires utilization of computational methods with different applicability and accuracy. A range of computational approaches is presented for molecules ranging from almost exact studies of the triatomic molecule of CuNO[1, 2] to polyfluorene[3] polymers containing thousands of atoms.

Detailed studies of well-defined small molecular systems such as CuNO for which a wide variety of accurate computational methods can be applied allow some principle insight into metal-ligand interactions, and ground and excited state properties. Such model systems are useful for testing the advantages and pitfalls of various theoretical models before studying larger complex systems. Ground state properties are benchmarked against available experimental and theoretical results using density functional methods (DFT), coupled-cluster methods, configuration interaction methods (CI), monte carlo CI (MCCI) and very accurate multi-reference CI (MRCI). For the study of photophysics and photodynamics of CuNO methods of time-dependent DFT, a range of response coupled cluster and state-averaged MCCI were applied. High order electron correlation methods are shown to be essential to correctly describe the state ordering.

In the second part, the importance of considering environmental effects, such as solvation and hydrogen bonding, in order to realistically model complex molecular systems is addressed. At first, in the excited states study of larger complexes of $[Cu(NH_3)_4]x(H_2O)_2$, $[Cu(CH3OH)_4]x(H_2O)_2$ and $[Cu(NH_2CH_3)_4]$, and in calculation of copper complexes reduction potentials providing basis for understanding of copper metalloproteins. Simulations including environmental effects have been carried out using implicit solvent models as well as quantum mechanical/molecular mechanical (QM/MM) methods.

In the last part, large-scale simulations of polyfluorene polymers are presented. Polyfluorenes have been intensively investigated for their interesting electrical and optical properties as promising materials for organic light-emitting diodes and solar cells. Therefore, using theoretical modelling as an invaluable tool assisting experiments can provide detailed understanding of relationship between monomer structure and bulk properties and can lead to rational design and tuning of structures exhibiting desired properties. Investigation of some of the bulk properties of polyfluorenes with different side-chain substituents were performed using molecular dynamics (MD) simulations. Interesting conformations of polyfluorenes produced by MD were further used in the subsequent QM and QM/MM calculations.

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	Presenter†	Title
P1	Dr Justyna Żurek	*Spectroscopy, charge- and energy-transfer pathways in diketopyrrolopyrrole (DPP) based organic materials:*
P2	Katie Emery	*Intramolecular formation of α-aryl ketone bonds between aryl halides and enolate anions via Electron Transfer*
P3	Divya Sharma	*Computational analysis of benzene interaction with crystalline ice surfaces: Ground and excited state investigations*
P4	Dr David Cheung	*Simulation of Complex Vesicles*
P5	Dr David McKay	*Computational Studies of C–X Activation (X = halogen) at Ru(II) Hydride Complexes via Nucleophilic Attack: A New, Potentially General Mechanism*
P6	Charis Georgiou	*Rational design of isoform specific ligands*
P7	Florimond Cumine	*C-C coupling of haloarenes with benzene via electron transfer reactions*
P8	Dr Jan Philipp Götze	*Carotenoids as chlorophyll Soret to Q band shortcut*
P9	Barry Mant	*Antimatter Chemistry*
P10	Georgios Gerogiokas	*Biomolecular hydration thermodynamics via grid cell theory aids prediction of ligand-protein binding affinities*
P11	Dr Alexandra Simperler	*NSCCS - National Service for Computational Chemistry Software*
P12	Kevin Pinto Gil	*Solvent Extension of the MDmix methodology and its impact on the quality of the predictions*
P13	Dr Russell McKinlay	*A TD-DFT and Coupled Cluster Response Theory Study of the Electronic Spectra of $Cr(CO)_6$, $Fe(CO)_5$ and $Ni(CO)_4$*
P14	Calum Waterson	*Design, synthesis and testing of reagents for high value mineral collection*
P15	Greg Anderson	*Organic Super-Electron-Donors: Initiators in Transition Metal-Free Haloarene-Arene Coupling*
P16	Nuno Almeida	*Challenging systems for quantum chemistry: intermolecular aggregates and inorganic excited states*
P17	Dr Asmaa Al-Baitai	*A computational study of the interaction of organic adsorbates with iron oxide surfaces*
P18	Peter Repiščák	*Multi-scale computational modelling of complex molecular systems: From CuNO to Polyfluorenes*
P19	Susanne Escher	*Basis set superposition error correction for reactive potential energy surfaces*
P20	Thomas Northey	*Ultrafast Imaging in Chemistry*
P21	Dr David Johnson	*Computational Study of Regioselective Gold(I) Catalysed Thioetherification of Allylic Alcohols*
P22	Dr Valerie Seymor	*Application of NMR Crystallography to the Investigation of Charge-Balancing Mechanisms in the Aluminophosphate STA-2*
P23	Daniel Cannon	*Revealing the Conformational And Binding Properties Of Gold Binding Peptide GBP1 With The Au{111} Surface*
P24	Dr Tanja van Mourik	*DNA base stacking involving adenine and 2-aminopurine*
P25	Kevin Carr	*Competition Studies of Ambiphilic Metal-Ligand Assisted C-H Activation*
P26	Leo Holroyd	*Mutagenic mispairing of 5-bromouracil*
P27	Adam Hardy	*Solvents for Cellulose - Insight from Computer Simulation*

P28	Dr Claire McMullin	*Mechanistic Investigations of C-H Functionalisation of pyrazoles with alkynes*
P29	Ivan Ramos Sasselli	*Parameterisation of the Fmoc Moiety for the CHARMM Force Field*
P30	Scott McKechnie	*High-throughput screening of organic chromophores for dye-sensitized solar cells*
P31	Elvira Bohl	*Photoionisation and Excitation Mechanisms of Fullerenes and Hydrocarbons after Femtosecond Laser Pulse Irradiation*
P32	José Antonio Garrido Torres	*Computational studies of metal-substrate interactions: Tetracene on a Rh(111) single-crystal surface*
P33	Dr Michael Doig	*Molecular dynamics study of automotive lubricants: linking molecular structure and friction*
P34	James McDonagh	*Predictions of Sublimation, Hydration and Solvation Free Energies for Crystalline Drug-like Molecules*
P35	Gary Scott	*Coarse Grained Approach for Determining the Self-Assemlbing of Peptides*
P36	Gaetano Calabro	*Investigation of Non-Additivity in Protein-Ligand Binding*
P37	Simon Hogan	*Computational Studies of Self-Assembled Monolayers*
P38	Remi Cuchillo	*Protein Druggability: the JEDI Approach*
P39	Prof. Michael Bühl	*Geometries, Energies and NMR Parameters of Fluorocyclohexanes from X-ray Crystallography and QM/MM Calculations*
P40	Dr Herbert Früchtl	*Formation of Bioinirganic Complexes by Corrosive Adsorption of (s)-Proline on Ni/Au(111) Surfaces*

[†]Poster numbers have been randomly assigned

Spectroscopy, charge- and energy-transfer pathways in diketopyrrolopyrrole (DPP) based organic materials: A computational study.

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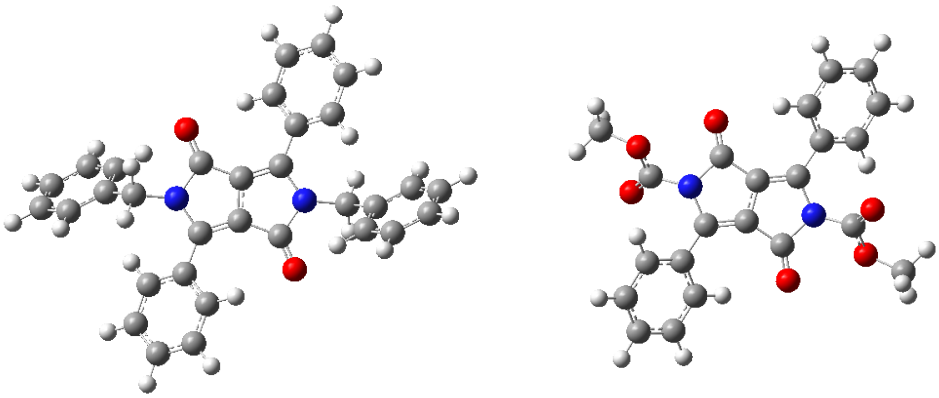
Diketopyrrolopyrrole (DPP) based systems, due to their optoelectronic properties, have been a subject of extensive study in recent years.[1, 2] By the choice of different donor-acceptor ligands one can tailor desired properties such as broad absorption wavelength range, stability or charge transport mobility of such organic materials. TD-DFT calculations on two new promising systems containing benzyl **(A)** and boc (*tert*-butyloxycarbonyl) **(B)** ligands have been performed to model their spectroscopic properties for both single molecule and intermolecular dimers. CASSCF relaxation pathway calculations on a model system have been performed and main energy crossing points in the singlet and triplet spin manifolds have been located. Reorganization energies of these systems have been calculated to determine their charge transport mobility properties.

(A) **(B)**



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Intramolecular formation of α-aryl ketone bonds between aryl halides and enolate anions via Electron Transfer

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Neutral organic electron donors have been utilized in biaryl couplings, with advantages over current techniques that these methods do not utilize costly metal reagents, which contaminate final products.[1-2]

Within the literature many publications report successful coupling between aryl halides and aromatic systems in presence of base using simple organic molecules such as phenanthroline, however the majority of these examples show aryl-aryl bond formation and only a few examples of alternative bond formations are reported.[2-3]

The intramolecular formation of *α*-aryl ketone bonds between aryl halides and enolate anions is being investigated.[4] The research involves a combination of experimental and quantum mechanical computational work.

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Computational analysis of benzene interaction with crystalline ice surfaces: Ground and excited state investigations

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Infrared observations on these icy mantles have shown water as the most abundant molecule in icy grain mantles. Polycyclic aromatic hydrocarbons (PAHs) are a particularly important class of aromatic molecule, which may account for up to 20 % of the galactic carbon and are likely to exist in the presence of water ice as either a part of the carbonaceous component of the dust grain itself or as a component of icy mantles. Benzene may be thought of as a prototypical PAH compound and is amongst the list of known interstellar molecules and water ice is a good representation of icy mantles on grains. Therefore, the computational study of the ground and excited states of the complexes of the benzene (Bz) with ice surfaces is of astrophysical relevance.

In our work, we focused on investigating ground state structures and energetics of complexes of Bz with crystalline ice surface. Two crystalline ice surfaces consisting of four binding sites each and respective Bz-ice complexes are optimized with ONIOM QM/MM methodology. Four binding sites consists of 3 d-H; 2 d-H 1 d-O; 1d-O 2 d-H; 3 d-O, where d-H and d-O denotes dangling hydrogen and dangling oxygen, respectively. We used DFT functional MO62X with 6-31++G** basis set as high level method for QM layer and AMOEBA force field for MM layer. Binding energies of Bz with ice surfaces are found to be dependent on the nature of binding sites that influence the energetics, with structure consisting of binding site (2 d-H 1 d-O atom) is of higher binding energy ≈ 10 kcal/mole. TD-DFT calculations are performed to investigate excited states of all eight ONIOM optimized ground state geometries of Bz- ice complexes using M062X functional and 6-31++G(d,p) basis set. Our results show that lowest singlet $\pi \rightarrow \pi^*$ electronic transition of benzene is red shifted under the influence of water cluster. Charge transfer (CT) states and diffuse Rydberg-type states are also found to play an important role in such complex systems.

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Simulation of complex vesicles

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Polymer vesicles, fluid-filled polymer sacs, have attracted great interest for a range of applications, such as drug delivery vehicles or miniature chemical reactors. Due to their similarity to biological cells they are often considered as minimal synthetic models of cells. Compared to naturally occurring systems synthetic vesicles are significantly simpler, lacking the much of the complexity of biological cells, which arises due to, e.g. the heterogeneous composition of the cell membrane or the attachment of proteins. Recently a number of experimental studies have begun to incorporate some of this complexity seen in biological systems, through the creation of multicomponent vesicles or vesicles armoured with colloidal particles. However, these experimental studies have not characterized in detail the microscopic changes in bilayer structure and properties.

This presentation will discuss two pieces of simulation work that try to address some of this missing information. In the first simple Monte Carlo simulations were used to study the packing of colloidal particles onto polymer vesicles. These simulations were able to reproduce the packing patterns seen in these experimental systems and to study the effect of surface charge density on the packing pattern. The second will address the effect of nanoparticles on the structure and phase separation in mixed polymer bilayers. Through establishing the relationship between the properties of the nanoparticles and the structure of polymer vesicles these simulation results will give insight into the directed assembly of polymer-nanoparticle structures, as well as giving insight into biological membranes.

Computational Studies of C–X Activation (X = halogen) at Ru(II) Hydride Complexes *via* Nucleophilic Attack: A New, Potentially General Mechanism

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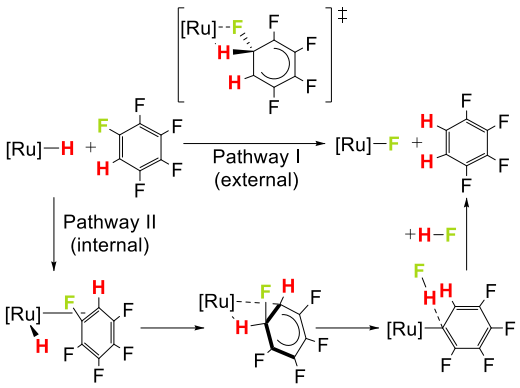
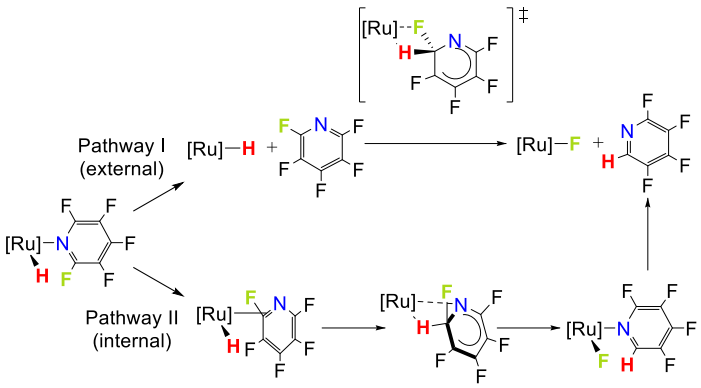
[b] *Department of Chemistry, University of Bath, Claverton Down, Bath BA2 7AY, UK*

Ru(II) N-heterocyclic carbene complexes of the type $[Ru(NHC)(PPh_3)_2(CO)(H)_2]$ (NHC = IMes (**1**), SIMes, IPr, SIPr) catalyse the hydrodefluorination (HDF) of C_6F_5H with an unusual *ortho*-selectivity to give 1,2,3,4-$C_6F_4H_2$.[1] Density functional theory (DFT) was used to locate two mechanisms based on a novel nucleophilic attack of a hydride ligand at the fluoroarene substrate (Scheme 1). Pathway I sees an external Ru–H···C–F hydride attack process while Pathway II features a stepwise internal process in which the rate-determining transition state (TS) involves formation of HF and a Ru-σ-fluoroaryl complex. Pathway II accounts for the unusual ortho-selectivity of this HDF process in the full experimental system (NHC = IMes).[2] Further DFT calculations investigated the extension HDF reaction to lower fluorinated $C_6F_{6-n}H_n$ (n = 2-5) substrates.[3]

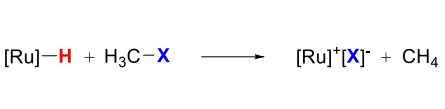


Scheme 1

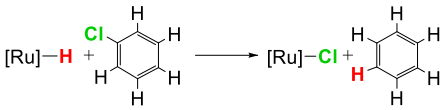


Scheme 2

The potential generality of the hydride attack mechanism is explored through HDF of fluoropyridines at **1** (Scheme 2), S_N2 reactions between *trans*-$[Ru(NHC)_2(PPh_3)_2(H)_2]$ (NHC = IMe_4) and CH_3X (X = I, Br, Cl, F) (Scheme 3) and C–X activation of XC_6Y_5 (X = Cl, Br, I; Y = H, F) at *mer*-$[Ru(PPh_3)_3(H)_2(H_2)]$, which sees room temperature bond activation even of chlorobenzene (Scheme 4).[4]



Scheme 3



Scheme 4

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Rational design of isoform specific ligands

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Cyclophilins are proteins able to catalyze the interconversion of *trans*/*cis* isomers of proline and belong to the peptidyl-prolyl isomerases family (PPIase). [1] In addition to their PPIase activity, cyclophilins have diverse biological roles and have been implicated in a number of different diseases such as HIV-1 and HCV. Although several cyclophilin inhibitors have been reported in the literature, none are able to inhibit with high specificity selected cyclophilin isoforms.

To facilitate the development of isoform-specific cyclophilin ligands, we are pursuing detailed studies of cyclophilin dynamics and binding thermodynamics using molecular simulations, biophysical assays and protein x-ray crystallography. Initial efforts are focussed on molecular dynamics (MD) simulations of the cyclosporine A (CsA) – cyclophilin A (CypA) complex, for which extensive biophysical measurements and structural data have been reported in the literature, with the goal to be the development of novel small molecule Cyp inhibitors. Models of the *apo* and *holo* CypA were set up using the Amber and AmberTools software and MD simulations were performed using Sire/OpenMM. [2, 3, 4] Analysis of the MD simulations are performed using custom scripts and the software package Gromacs. [5]

To facilitate the development of novel Cyp inhibitors, x-ray crystallographic studies were carried out using small fragments, for which binding affinities were reported from Surface Plasmon Resonance (SPR) experiments. Intermolecular interactions of CypA complexes observed from x-ray crystallography and MD simulations have been characterised. Those interactions include: hydrogen bonding interactions between the ligand and protein, interactions with water molecules. Efforts towards the computation of binding free energies and changes in conformational entropies will be reported.

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C-C coupling of haloarenes with benzene via electron transfer reactions

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The use of organic molecules as a replacement of transition metals in electron transfer reactions is a recent exciting development addressing the needs of more environmental friendly chemistry.

These easy feasible and cheap organic molecules are capable of undertaking reactions that were usually achieved by reactive metals such as Palladium.

The C-C coupling of haloarenes with benzene, used as a solvent, is now made easily feasible by undertaking an electron transfer reaction which starts a catalytic cycle conducted by the successive formations of radicals and electron transfers.

This poster will describe experimental and computational studies in this area.

Carotenoids as chlorophyll Soret to Q band shortcut

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In this study, we investigated the differences that occur upon exchange of the carotenoid xanthophylls violaxanthin (Vx) and zeaxanthin (Zx) in a light harvesting complex II (LHCII) xanthophyll binding site. This exchange is supposed to be a reaction to plant light stress, leading to Zx via the so-called xanthophyll cycle.[1] Vx and Zx have been in the past investigated by computational approaches, leading to the conclusion that the differences in terms of photophysics are likely minute.[2] Here, we used an approach that embedded the xanthophyll together with the spatially closest chlorophyll b (Chl) unit within a rigid shell of LHCII amino acids.[3] Within this frozen protein shell, we allowed the chromophores to relax in the bright xanthophyll excited state, allowing us to explore post-excitation effects. Geometries of the chromophores were computed using (TD-)CAM-B3LYP/6-31G*, the shell was treated with PM6 in an ONIOM scheme. The TD-DFT spectra were supported and expanded using a multiconfigurational DFT approach (DFT/MRCI).[4]

Vx and Zx apparently exhibit post-excitational differences: The Zx compound relaxes energetically below the Chl Q band (about 600 nm), while the Vx bright state minimum is energetically still above. Consequently, it appears that Vx is more likely to donate energy to the Chl Q band, which acts as the active energy region for photosynthetic processes. Furthermore, from dipole orientation analysis, it appears that both Vx and Zx are able to acquire population from the Chl Soret band (about 400 nm). This would allow Vx and Zx, or likely carotenoids in general, to de-populate the Soret band of Chl – and thus allow the Chl to become Q band excited by another excitation event or energy back-transfer, with carotenoids effectively serving as a Soret to Q band shortcut.

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Antimatter Chemistry

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Experimental work into the properties of antimatter is set to answer fundamental questions in physics[1] and has inspired new theoretical work into matter-antimatter interactions[2]. These interactions are necessary for producing antimatter systems and are responsible for their destruction. In this project the primary focus is on antimatter collisions with molecular hydrogen species. Matter-antimatter chemical reactions have been observed experimentally[3] and are also a major source of trapped antimatter destruction, thus, a better understanding of these processes is important. Here we present preliminary work on the potential energy surfaces (PES) of antiproton interacting with H_2/H_2^+ which have been calculated using *ab initio* quantum chemistry techniques. We describe methods which are being developed to carry out fully converged quantum elastic, inelastic and reactive scattering calculations for these systems utilizing the S-matrix version of the Kohn variational principle.[4]

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Biomolecular hydration thermodynamics via grid cell theory aids prediction of ligand-protein binding affinities

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Prediction of binding free energy can aid acceleration of the drug discovery and optimisation process. However, many current predictors do not account for the hydration thermodynamics. A novel, efficient methodology has been developed to quantify water energetics through an analysis of explicit solvent molecular simulations of organic and biomolecular systems. The approach, grid cell theory (GCT), relies on a discretization of the cell theory methodology on a three-dimensional grid to spatially resolve the density, enthalpy and entropy of water molecules in the vicinity of system(s) of interest for qualitative and semi-quantitative analyses [1].

Using GCT we investigate ligand-protein systems by computing numerical estimates of the energetics of desolvation from suitable thermodynamic cycles. This involves simulating protein, ligand and complex structures of your system of interest, in our case of a congeneric series of Hsp90 ligands [2]. The hydration energetics of each state gives a physically intuitive understanding of the water reorganisation cost of binding incurred by the protein and ligand desolvation energies as well as complex solvation energy. These thermodynamic states can be visualised as isosurfaces allowing identification of stable and unstable water sites. These GCT desolvation terms coupled with interaction energies between the protein and ligand can be used to compute a predictive protein-ligand score which should prove useful during ligand optimisation.

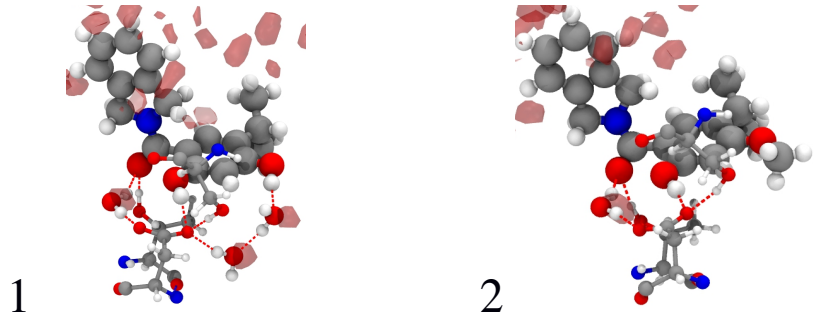

Figure. The spatial resolved grid of the hydration ΔG in the protein-ligand structures are shown as isosurfaces. ASP 93, THR 184, and SER 52 are shown in smaller VDW spheres while the selected ligands, **1 and 2**, are shown in larger VDW spheres. Hydrogen bonds are displayed as red dotted lines while the red isocontours of each hydration grid is generated using an isovalue of -16 kcal mol^{-1} $Å^{-3}$.

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NSCCS – National Service for Computational Chemistry Software

The EPSRC UK National Service for Computational Chemistry Software (NSCCS) at Imperial College London provides access to software, specialist consultation, computing resources and software training to support UK academics working across all fields of chemistry.

The NSCCS hardware is based and managed by our partner at the Rutherford Appleton Laboratory (RAL) of the Science and Technology Facilities Council (STFC). The NSCCS Cluster is called Columbus. Columbus is a 512-cores Silicon Graphics Altix UV 1000 and has a memory of 2TB with 10Gb network. CPU: 64 x Intel E7-8837, 2.66GHz, 24MB cache, 8 cores per node. At the moment the NSCCS hosts 35 software packages.

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Solvent Extension of MDmix methodology and its impact on the quality of the predictions

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Binding hot spots are points on the protein surface displaying high propensity to interact with other molecules. They can be found in protein-protein interfaces as well as on ligand binding sites, where the hot spots inferred from the protein structure should overlap with pharmacophores derived from the alignment of multiple ligands. Molecular Dynamics (MD) simulations with explicit aqueous/organic solvent mixtures (MDmix) have been proposed as a means to identify binding hot spots.(1,2) This computational experiment is analogous to solvent mapping carried out by X-ray crystallography and NMR, which are well known and accepted means to detect binding sites and their corresponding hot spots.(1)

MDmix simulations can use a wide range of small organic molecules as co-solvents, hence it is important to know if the information provided is redundant or can be complementary. In this work, we first expand the set of organic molecules to be used in MDmix in order to cover a wide range of chemical moieties. We then proceed to evaluate the information provided by MDmix simulations of these solvents on beta-secretase 1 (BACE-1), comparing the results with the exhaustive structural and pharmacological information available for the system. The most important pharmacophoric points defined by the ligands coincide with the most intense binding hot spots predicted by MDmix, and we find a large degree of overlap between different atom types (e.g. aromatic vs. aliphatic), but also some notable differences. This allows us to propose a ranked list of solvent types to be used in MDmix studies, to gain the maximal amount of information with the minimum number of simulations.

Finally, we have identified some currently unexploited hot spots and selected compounds for in vitro testing that should be able to interact with, and gain binding affinity from, those points.

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A TD-DFT and Coupled Cluster Response Theory Study of the Electronic Spectra of $Cr(CO)_6$, $Fe(CO)_5$ and $Ni(CO)_4$

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Binary transition metal carbonyls have been intensely studied over the years regarding their structure and reactivity and they are paradigm complexes for the study of metal-carbonyl bonding. Their electronic spectroscopy and photochemistry, however, have presented many challenges, both theoretically and experimentally, due issues such as system size, multi-configurational electronic states, and their broad, featureless electronic spectra with a high density of electronic states of different chemical character within a narrow energy range [1].

We present our efforts to study the electronic spectra of three binary carbonyls $Cr(CO)_6$, $Fe(CO)_5$ and $Ni(CO)_4$ using both TD-DFT and coupled cluster response theory (CC2, CCSD, CCR(3), CC3). Atomic natural orbital (ANO) all-electron basis sets have also been compared to effective core potential ones. These results are compared with previous experimental and theoretical results [2,3]. Our results explain many features of the electronic absorption, although these molecules are shown to represent extreme challenges for both TD-DFT and correlated response methodologies.

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Design, synthesis and testing of reagents for high value mineral collection

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Design, synthesis and testing of reagents for high value mineral collection

We present a Density Functional Theory study of the binding of small organic molecules to high value mineral surfaces. Froth flotation is a physicochemical process designed to separate finely ground solids on the basis of their relative water wettabilities (hydrophobicities). Common industrial practice involves adding 'collectors', small organic molecules with a mineral binding head group and a short chain aliphatic tail, into the flotation mixture to find and promote the recovery of high value minerals by binding to the mineral and modulating its surface hydrophobicity. We are using Density Functional Theory, combined with electrochemical and other experimental validation techniques, to gain a molecular level understanding of the binding of these collectors onto common high value minerals as well as unwanted minerals with the aim of designing new, more efficient collectors.

Organic Super-Electron-Donors: Initiators in Transition Metal-Free Haloarene-Arene Coupling

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Within both industrial and academic settings, the coupling of two aryl moieties is a process of significant synthetic value. To achieve such transformations typically requires the use of expensive transition metal catalysts that cannot always be recovered from reaction mixtures. As such, the investigation of biaryl coupling reactions without any requirement for such catalysts has been of key interest amongst chemists.

Outlined in this work is the ability of a number of reagents, termed incorrectly as “catalysts” or “ligands” within the literature, to form organic super electron donors *in situ* following reaction with a strong base. These electron donors are capable of reducing an aryl iodide to its radical anion, which can then dissociate to the corresponding aryl radical following the loss of iodide. Provided that there is sufficient base present, a cyclic radical pathway leads to the formation of biaryl products.

Support for experimental observations has been obtained through the application of Density Functional Theory to probe both the energetics and feasibility of proposed mechanistic pathways. Results from these studies agree with the requirement for high temperature reaction conditions, and suggest such conditions are required in order to drive the donor-forming reactions forward.

Challenging systems for quantum chemistry: intermolecular aggregates and inorganic excited states

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Supramolecular structures have grown in importance in recent years due to their potential applications as advanced functional materials. The fine-tuning of these structures allows building up higher hierarchical superstructures with very diverse and interesting properties. Theoretical calculations using DFT (Density Functional Theory) investigating the self-assembly of p-{[4,6-Bis(p-carboxybenzoylamino)-1,3,5-triazin-2-ylamino]carbonyl}benzoic acid hydrogel were carried out. A bottom-up approach for this kind of systems is used to characterize the multichromophoric self-assembly of pH dependent gels[1], and detail their responses to light.

A strong π-π interaction is fundamental to keep these structures together as well as strong hydrogen bonding. In biological structures these types of interactions play a major role. A good example is the intercalation of porphyrins with DNA. The structure of d(CGATCG) - CuTMPyP4 could help explain the aspects of electron-transfer processes that occur in DNA. The complex is stabilized by electrostatic interactions between the nitrogen atoms in the porphyrin and the negatively charged phosphate groups. This phenomenon also causes an increase of the specific viscosity in solution of the DNA. A theoretical study using DFT and QM/MM (ONIOM) of this biological system is also presented[2].

Excited states of inorganic systems can be extremely challenging for conventional methods of quantum chemistry, mostly due to strong correlation, degeneracy and near-degeneracy problems, in addition to a large density of states. A benchmark study of the electronic excited states of a range of complexes has been carried out using a range of coupled cluster response methods (CCS, CC2, CCSD and CC3) and time-dependent (TD)-DFT. A range of both all-electron and ECP basis sets are also used. These calculations reveal the effect of systematically improving the treatment of electron correlation. The calculated results are compared with each other and experimental values where available. Finally, several pathological features of popular response methods have been identified that are not apparent in organic systems[3,4].

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A computational study of the interaction of organic adsorbates with iron oxide surfaces

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Atomistic simulation techniques were used to investigate the adsorption of two organic molecules, namely methanoic acid and hydroxyethanal, to a range of hematite (α-Fe_2O_3) and maghemite (γ-Fe_2O_3) surfaces. Hydroxyethanal provides us with information about the effect of a larger, more flexible molecule by increasing the chain length which also affects the functional group. We will consider two initial configurations of hydroxyethanal, a staggered and eclipsed conformer, although the molecules are free to rotate during the simulations. Our results show that the calculated adsorption energies of the two conformers of hydroxyethanal to all dehydrated surfaces is much stronger than the adsorption of methanoic acid, owing to the presence of multiple interactions between the surface and the hydroxyethanal molecule, due to its greater flexibility and span. On the most reactive surfaces, the hydroxyethanal molecule is able to coordinate to the surface by bridging between two surface iron atoms through both its carbonyl oxygen atom and hydroxyl oxygen atom

These findings have given an understanding into interactions at the atomic level which indicate that modeling techniques should be capable of predicting adsorption behavior and designing collector molecules.

Multi-scale computational modelling of complex molecular systems: From CuNO to Polyfluorenes

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Theoretical investigation of complex systems of different system size often requires utilization of computational methods with different applicability and accuracy. A range of computational approaches is presented for molecules ranging from almost exact studies of the triatomic molecule of CuNO[1, 2] to polyfluorene[3] polymers containing thousands of atoms.

Detailed studies of well-defined small molecular systems such as CuNO for which a wide variety of accurate computational methods can be applied allow some principle insight into metal-ligand interactions, and ground and excited state properties. Such model systems are useful for testing the advantages and pitfalls of various theoretical models before studying larger complex systems. Ground state properties are benchmarked against available experimental and theoretical results using density functional methods (DFT), coupled-cluster methods, configuration interaction methods (CI), monte carlo CI (MCCI) and very accurate multi-reference CI (MRCI). For the study of photophysics and photodynamics of CuNO methods of time-dependent DFT, a range of response coupled cluster and state-averaged MCCI were applied. High order electron correlation methods are shown to be essential to correctly describe the state ordering.

In the second part, the importance of considering environmental effects, such as solvation and hydrogen bonding, in order to realistically model complex molecular systems is addressed. At first, in the excited states study of larger complexes of $[Cu(NH_3)_4]x(H_2O)_2$, $[Cu(CH3OH)_4]x(H_2O)_2$ and $[Cu(NH_2CH_3)_4]$, and in calculation of copper complexes reduction potentials providing basis for understanding of copper metalloproteins. Simulations including environmental effects have been carried out using implicit solvent models as well as quantum mechanical/molecular mechanical (QM/MM) methods.

In the last part, large-scale simulations of polyfluorene polymers are presented. Polyfluorenes have been intensively investigated for their interesting electrical and optical properties as promising materials for organic light-emitting diodes and solar cells. Therefore, using theoretical modelling as an invaluable tool assisting experiments can provide detailed understanding of relationship between monomer structure and bulk properties and can lead to rational design and tuning of structures exhibiting desired properties. Investigation of some of the bulk properties of polyfluorenes with different side-chain substituents were performed using molecular dynamics (MD) simulations. Interesting conformations of polyfluorenes produced by MD were further used in the subsequent QM and QM/MM calculations.

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Basis set superposition error correction for reactive potential energy surfaces

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In theoretical studies of intermolecular interactions, basis set superposition error needs to be considered. A common scheme for correcting it is the counterpoise method.

When the chemical identity of interacting moieties is unclear, as in reactive processes, switching between different counterpoise schemes can lead to a discontinuous potential energy surface.

A geometry-based variation of this method combining two counterpoise schemes was developed for reactive potential energy surfaces to correct for basis set superposition error in these cases.

This problem arose when investigating the interaction of ammonia and hydrogen astatide using coupled cluster (CCSD(T)) calculations.[1] These were built upon and the new scheme was implemented and tested on this system. Two different mathematical approaches for combining counterpoise corrections were employed, showing very similar results and removing the discontinuity in the potential energy surface.

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Ultrafast Imaging in Chemistry

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A new generation of x-ray sources, x-ray free electron lasers (XFEL) boast unprecedented photons/pulse (10^{12}) with ultra-short pulse lengths (approx. 20 fs). This gives rise to new experiments, not only in crystal-free or nano-crystal imaging of biomolecules and functional materials but also in the field of time-resolved diffraction.

New theory will be presented using *ab initio* multi-configurational Ehrenfest trajectories (AIMCE, K. Saita, D.V. Shalashilin, J. Chem. Phys. 2012) combined with x-ray scattering theory to obtain time-evolving diffraction patterns.

A comparison is made to a recent experiment (Feb. 2014) at LCLS which probed a time-evolving pattern of a photoinduced ring-opening reaction of 1,3-cyclohexadiene after excitation by a UV-laser pump to form 1,3,5-hexatriene.

Computational Study of Regioselective Gold(I) Catalysed Thioetherification of Allylic Alcohols

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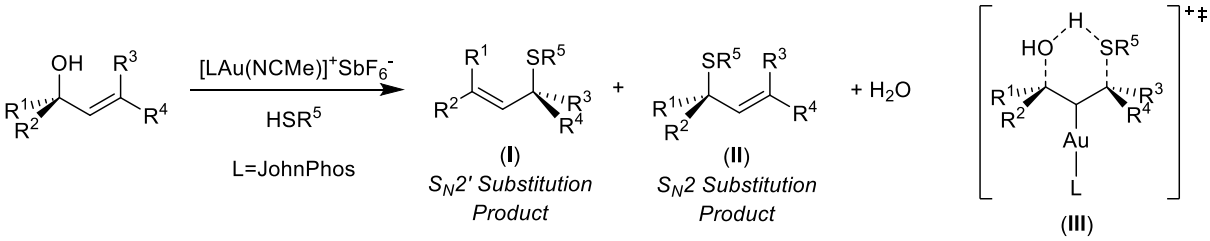
Gold catalysis has seen a significant increase in interest in the last 15 years.[1] In particular the Lewis-acidic Au(I) centre is known to activate carbon-carbon multiple bonds allowing for nucleophilic attack. Previous work has investigated the etherification of allylic alcohols with *O*-based nucleophiles with an Au(I) catalyst.[2] Here, the results of a computational study of the related thioetherification will be presented.



The thioetherification reaction involves formation of a sulfur-carbon bond at the C3 position, in what is classed a formal S_N2' nucleophilic substitution. This has been shown to proceed with excellent regioselectivity in experimental studies, which show a preference for the S_N2' product (**I**). However this is not without exception, for example when $R^1 = R^2 = H$ and $R^3 = R^4 = Me$ the S_N2 substitution product (**II**) is instead preferred.

Density functional theory (DFT) is used to study the reaction, and it is shown that the S_N2' mechanism proceeds *via* an external attack of thiophenol at the C3 position of the allylic alcohol. The key transition state (**III**) involves the formation of a carbon-sulfur bond and loss of water through proton transfer to give (**I**). A second S_N2' step can then occur to form the S_N2 product (**II**) directly from (**I**), where a second thiol nucleophile attacks at the C3 position. The computed barriers suggest that both S_N2' steps are readily accessible and that the regioselectivity is ultimately dictated by the thermodynamic stability of the products.

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Application of NMR Crystallography to the Investigation of Charge-Balancing Mechanisms in the Aluminophosphate STA-2

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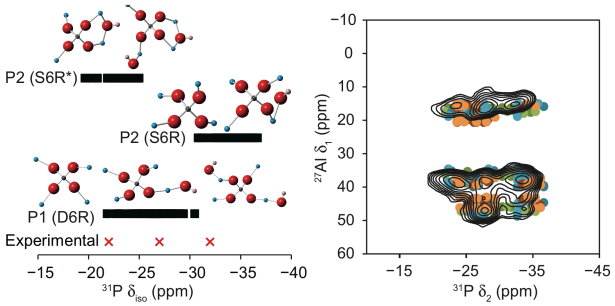
Zeolitic materials, including aluminosilicates and aluminophosphates, are an important class of microporous materials, with applications in medicine, catalysis, separation and ion exchange. They consist of frameworks containing pores and channels of molecular dimensions, allowing chemistry to take place at their internal surface and giving rise to many useful properties. Solid-state NMR is very suitable for the study of local environments in microporous materials, as it can be used to study both the framework (^{27}Al, ^{31}P, ^{17}O), including extra-framework species, and encapsulated template (^{13}C, ^{15}N, ^{1}H), used in the synthesis. The aluminophosphate framework STA-2 has been studied by a combination of multinuclear solid-state NMR and density functional theory (DFT) calculations.[1] In the as-prepared material, the positive charge of the organocation template is balanced either by hydroxyls groups coordinated to the framework, or by the negative charge introduced by the substitution of M^{2+} (for example Mg^{2+} or Zn^{2+}) for Al^{3+}. NMR parameters have been calculated for a range of models containing different positions for charge-balancing anions and different levels and positions of cation substitution, using periodic DFT approaches. These aid spectral assignment and interpretation, thereby providing insight into the local structure and order. ^{27}Al MAS NMR spectra show Al is present in both tetrahedral and five-fold coordination, with the ratio dependent on the charge-balancing mechanism. For ^{31}P, the isotropic chemical shifts depend not only on the topologically-distinct site in the framework, but also on the next-nearest-neighbour environment, $P(OAl)_{4-n}(OM)_n$ and the coordination mode of the hydroxyls.



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Revealing the Conformational And Binding Properties Of Gold Binding Peptide GBP1 With The Au{111} Surface

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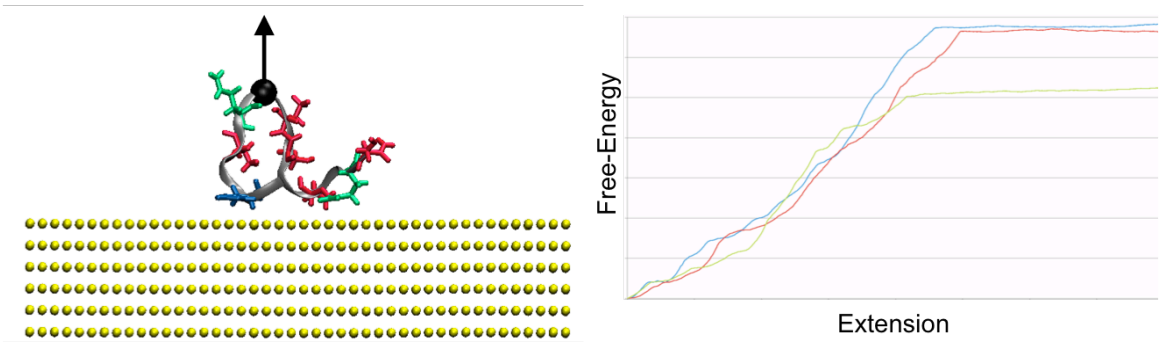
Gold binding peptides have been successfully employed in the controlled synthesis of gold nanoparticles.[1-2] One of the first peptides to be identified for its gold-binding properties was the sequence (MHGKTQATSGTIQS), known as GBP1[3]. Many hypotheses exist as to why this sequence displays such high affinity, and indeed specificity, for gold. However, no study comprehensively examines the binding free energy of this peptide and how certain moieties influence its adsorption strength. Therefore, we conduct a thorough investigation of the conformational properties of GBP1 and its binding affinity, revealing the quantitative impact of particular amino acids on these characteristics. The utilisation of advanced computational techniques[4] allows us to look at the key structural and energetic features of gold-binding peptides, which may facilitate rational design in bio-metallic recognition.



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DNA base stacking involving adenine and 2-aminopurine

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Stacking interactions are one of the main factors in stabilising DNA, and a detailed understanding of the stacking between DNA bases is therefore of much relevance to increasing our knowledge of the stability of DNA structures. In addition, stacked DNA base associates are in themselves of considerable scientific interest as model systems to study the inherent nature of π stacking. In this work, the structures and interaction energies of stacked base pairs consisting of adenine (A) and 2-aminopurine (2AP) were studied. 2AP is an analogue of the DNA base A and is widely used as a fluorescent probe in studies on DNA conformation and DNA-protein interactions. We are interested in how the presence of 2AP in the stacked dimers affects the structure and stacking energy. A/A, 2AP/2AP and mixed A/2AP stacked structures were determined at the M06-2X/6-31+G(d) level of theory by systematic scans of the potential energy surfaces. The potential energy surfaces are characterised by many close minima separated by low energy barriers.

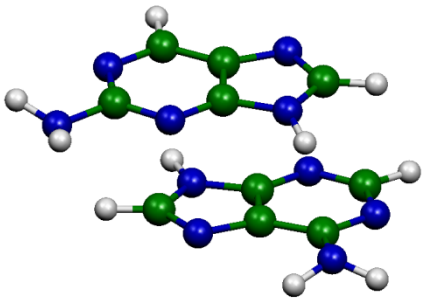

Fig. 1 - One of the A/2AP minima

Competition Studies of Ambiphilic Metal-Ligand Assisted C-H Activation

Kevin J. T. Carr[a], Barbara Villa Marcos[b], Stuart A. Macgregor[a], and David L. Davies[b]

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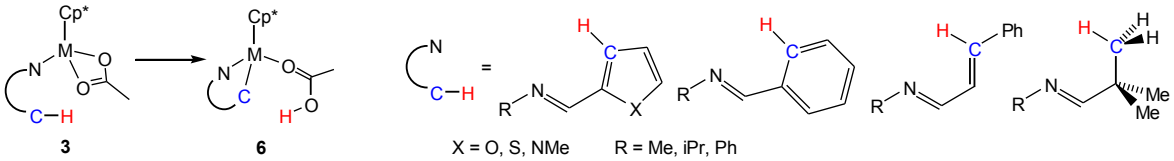
Direct functionalisation of a C-H bond to give C-C or C-Y bonds is a desirable goal in synthetic chemistry as it allows for building complex frameworks without the use of leaving groups. The relatively inert nature of the C-H bond makes this process a challenge; however, this can be achieved via an ambiphilic metal-ligand assisted (AMLA) process at a range of metals (M = Pd, Rh, Ru, Ir) in combination with a chelating base such as acetate (Scheme 1).[1]



Scheme 1 – AMLA C-H activation and substrates examined by DFT.

In order to understand the factors controlling the AMLA process, we have conducted a joint experimental and DFT study into the competition for C-H activation between a variety of $[Cp^*M(OAc)(N\cap CH)]^+$ species (M = Rh, Ir; N∩CH defined in Scheme 1). Differences in substrate preference between Rh and Ir can be explained by a change from thermodynamic control observed in Rh to kinetic control observed in Ir. This is caused by the high stability of the Ir product **6** leading to an irreversible reaction.

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Mutagenic mispairing of 5-bromouracil

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5-Bromouracil (BrU), a structural analogue of thymine, is a potent experimental mutagen. It exerts its mutagenic effect by mispairing with guanine instead of adenine in DNA, causing both AT→GC and GC→AT point transitions. This is analogous to the thymine-guanine mispairing which was proposed by Watson & Crick as the cause of spontaneous mutations involving the natural bases.

Spontaneous mispairs are generally assumed to involve minor tautomers of one base or the other – the so-called "rare tautomer hypothesis" (Figure 1). It follows that the enhanced mutagenicity of base analogues may be due to their greater propensity for tautomerisation.[1] However, experimental evidence for this hypothesis in relation to BrU is hard to come by.

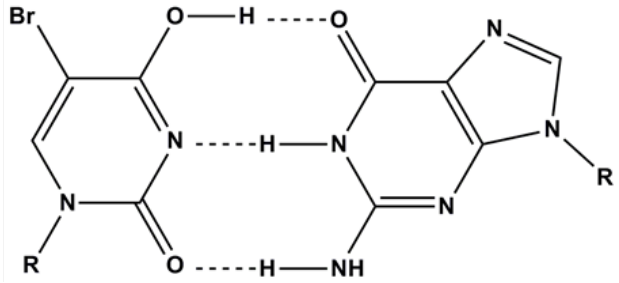

Figure 1 – Potentially mutagenic mispair between the minor (enol) tautomer of 5-bromouracil (left) and the major tautomer of guanine (right). Despite the mismatch the bases are in Watson-Crick geometry.

The poster presents computational research into several lines of enquiry – to what extent does solvation in water nanodroplets influence the tautomeric constant of BrU, as assessed by various functionals; what is the role of water in the dynamical tautomerisation process (i.e. proton transfer), as modelled by CPMD; and can the abundance of BrU-G mispairing be better explained by enhanced intrastrand base stacking of BrU, as measured by double-hybrid functionals and df-LCCSD(T).[2]

The results broadly support the rare tautomer hypothesis.

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Solvents for Cellulose - Insight from Computer Simulation

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The development of greener solvents for cellulose requires thorough understanding of the molecular level processes that govern the dissolution process. We combine experiments and computer simulation to provide this insight.

The interactions between cellulose chains are dominated by hydrogen bonding. Thus, to separate the chains from each other, these hydrogen bonds need to be disrupted. This requires attack of the donor or acceptor atoms with compatible functional groups of the solvent. A number of solvents have been found to achieve this, but they are generally environmentally harmful.

To design better solvents we need to understand how solvents disrupt cellulose/cellulose hydrogen bonds. This project uniquely combines solvent tests, high-resolution solid-state NMR and computer simulations. This allows to link microscopic structural information to macroscopic function and to take advantage of the complementary microscopic insight from experiment and simulation.

Mechanistic Investigations of C—H Functionalisation of pyrazoles with alkynes

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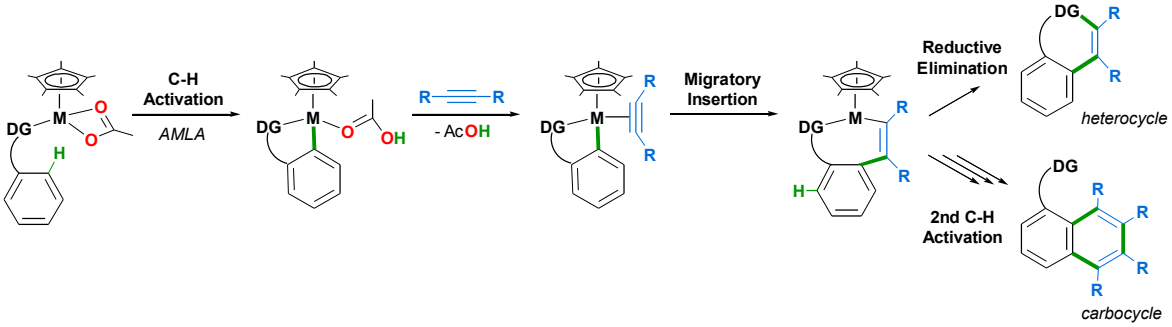
Catalytic C—H functionalisation has shown potential as a new route to many desired synthetic compounds by forming new C—C and C—Y bonds (Y = O, N). However, current understanding of the mechanisms involved in such reactions is limited - yet key to a rational basis for developing efficient and selective catalytic systems.

Previously, we have shown that C—H activation can occur by a bound acetate group to a metal centre (M = Pd, Ru, Rh and Ir) via an ambiphilic metal ligand assisted (AMLA) process.[1-2] This intramolecular step is now well established for a range of substrates with heteroatom directing groups (DG), leading to the synthesis of heterocycles or carbocycles (Scheme 1), depending on the nature of the DG and insertion partner.



Scheme 1 – C—H Functionalisation reaction pathway for a phenyl substituted directing group substrate and an alkyne (RC≡CR) with a [Cp*M] complex

In conjunction with experimental studies from the Davies group, DFT calculations are used to further elucidate the key steps within the catalytic cycle and reproduce observed mechanistic data. The focus of work presented will be on phenyl-substituted pyrazole DG substrates coupling with an alkyne insertion partner (RC≡CR) to form new C—C bonds, using a group 9 metal catalyst, [Cp*M], when M = Rh or Ir.

Whilst C—H activation is often thought to be rate limiting, our results suggest it is the migratory insertion and reductive elimination steps that can determine product selectivity and reaction viability.

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Parameterisation of the Fmoc Moiety for the CHARMM Force Field

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CHARMM Force Field (FF) has been widely used for Molecular Dynamic (MD) simulations of proteins and peptides in order to gain knowledge about the processes that is not accessible through experimental techniques.

In recent years, CHARMM use has been extended to the study of the self-assembling properties of short peptides. These peptides are known to form well-ordered nanostructures driven by intermolecular interactions. MD simulations can be a powerful tool in understanding the process and final structures in a level that is not accessible experimentally.

Although self-assembly is more facile in peptides of at least ten amino acids, the ability of shorter peptides to spontaneously form nanostructures can be improved with the addition of aromatic groups. The inclusion of an aromatic end-group enhances self-assembly through extra π-stacking interactions. Several di- and tripeptides bound to the Fmoc moiety (9-Fluorenylmethyloxycarbonyl) are known to self-assemble into nanostructures with interesting properties.

In this project the Fmoc moiety is parameterised for the CHARMM FF in order to be able to apply MD simulations to Fmoc-peptides self-assembling systems to improve the design process of these promising new materials.

High-throughput screening of organic chromophores for dye-sensitized solar cells

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The dye-sensitized solar cell (DSSC) is a low cost and technically promising alternative to the conventional silicon-based photovoltaic device. Lower efficiency levels are a major drawback but an increase of only a few percent would afford a highly competitive solar-cell technology. At the heart of the cell is a dye molecule which is responsible for light capture and electron injection. The experimental search for novel dye molecules is expensive, time consuming and often chemically biased. On the other hand, high-throughput computational screening is cheap, fast and can search a large portion of chemical space. However, there are a number of fundamental problems associated with the accurate determination of dye properties on the large-scale. First of all, the molecules are often highly flexible and possess a complex potential energy surface with multiple minima. A so called NP-hard problem, finding low-energy structures requires navigating a complex space. We address this problem by considering what information can be obtained from crystallographic data and what shortcuts can be made in the search for low-energy structures. In addition, there is no consensus on the optimal method for determining the electronic structure of molecules, with particular difficulty for modeling the excited state. We consider the capabilities of DFT and TDDFT by comparison with experimental and higher-level computational results. More specifically, the alignment of ground and excited state energy levels and the calculation of the overall absorption profile. The general framework for the batch processing of molecules that combines quantum chemistry and cheminformatics tools will also be outlined.

Photoionisation and Excitation Mechanisms of Fullerenes and Hydrocarbons after Femtosecond Laser Pulse Irradiation

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Fullerenes are good model systems to study the excitation and ionisation mechanisms of complex molecules. Femtosecond photoelectron spectroscopy of fullerenes, like C_{60} and C_{70}, revealed highly excited Rydberg-like states.[1] The photoelectron spectra (PES) showed a thermal electron background and a peak structure superimposed on it below kinetic energies corresponding to the photon energy.[1] The peak structure could be assigned to one-photon ionisation of diffuse low-angular momenta states, so-called superatom molecular orbitals (SAMOs) centred on the hollow fullerene core, based on photoelectron angular distributions (PADs) and TD-DFT calculations.[1] Further studies on the fullerene species C_{82} and $Sc_3N@C_{80}$ showed PES and PAD with similar features.[2] The peaks become less prominent compared to the thermal electron background for increasing molecular size and decreasing symmetry and are almost absent for the endohedral species.[2] Therefore the thermal electron emission seems to be the main ionisation mechanism for larger and more complex molecules at these excitation conditions.[2] The relative photoionisation probabilities of the s-SAMO to p-SAMO were analysed for photon energies from 2-3.5 eV and showed good agreement with theoretical calculations.[3]

Quantum mechanical studies on a series of polycyclic aromatic hydrocarbons (PAH) revealed similar Rydberg-like molecular orbitals in analogy to the SAMOs in fullerenes and will be discussed. The binding energies of the s-state and the p_z-state show a decreasing trend with increasing molecular size.

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Computational studies of metal-substrate interactions: Tetracene on a Rh(111) single-crystal surface

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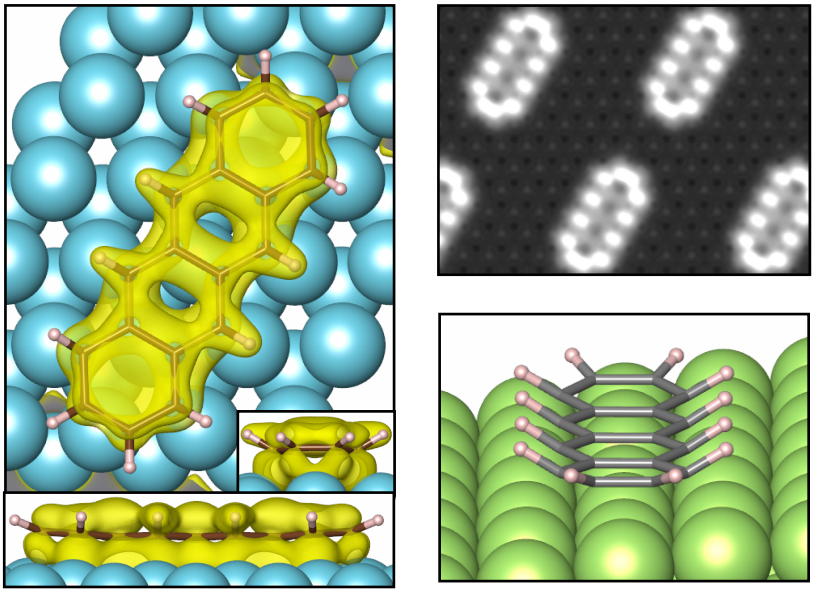
π-conjugated systems are important components of organic-electronic devices and photovoltaic cells [1,2]. Hence, the detailed understanding of their interaction with a variety of relevant supports, both theoretically [3] and experimentally [4], is central to our ability to improve and develop novel functional devices. In this context, the adsorption behaviour of π-conjugated molecules on a wide range of metals has recently spurred intensive scientific interest [5].

In this research, we focus our studies on the interaction of tetracene with a single-crystalline Rh(111) surface. Adsorption energies at different surface sites, computed from Density Functional Theory (DFT), are discussed and compared with Scanning Tunnelling Microscopy (STM) and High-Resolution Electron Energy Loss Spectroscopy (HREELS) experimental results, with a view to combine theoretical (*Scheme 1*) and empirical insights. The comparison of geometry, electron density, and charge variations aid in a better understanding of the molecule-substrate interaction.



Scheme 1. *Electron density (left) and optimised structure (bottom right) for the most stable adsorption site for tetracene on Rh(111). Simulated STM image for the same adsorption site (top right).*

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Molecular dynamics study of automotive lubricants: linking molecular structure and friction

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Lubricant oils are used to reduce friction and wear in a wide range of industrial and mechanical processes. Lubricant additives play a vital role in the oils' overall performance, particularly surface-active additives which can significantly affect the tribological properties of solid surfaces. However, there is insufficient understanding of the link between the atomic-level structure of tribofilms and the macroscopic properties such as friction, to direct the development of new lubricant formulations.

Using large-scale molecular dynamics simulations, we investigate a range of lubricated systems, studying the structural properties of surface-adsorbed tribofilms on metal-oxide surfaces, and how they vary with temperature, pressure, surface coverage and shear rate. Several important trends are identified linking molecular isomerism and architecture with the structure and stability of the adsorbed films. In addition, the simulation results are used to gain insight on recent experimental measurements of film structure. Some examples of the systems studied include oleic acid and stearic acid films lubricated by squalane and hexadecylamine films lubricated by dodecane, both adsorbed on iron oxide surfaces.

The friction coefficients in these systems are computed and analysed with reference to the structure of the adsorbed films, to yield new insights on the intimate link between the molecular properties of lubricants and the macroscopic frictional properties of lubricated systems.

Predictions of Sublimation, Hydration and Solvation Free Energies for Crystalline Drug-like Molecules

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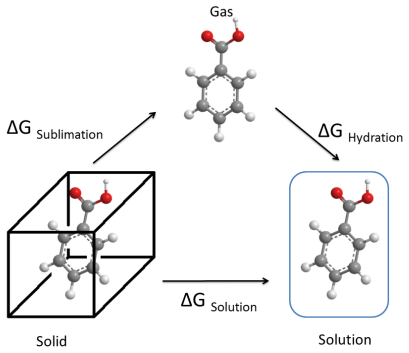
Accurate predictions of solubility save time and money in the drug development process by providing early-stage viability screening of drug candidates. QSPR models show much promise for high-throughput virtual screening and provide valuable information quickly; however, such models can lack physical insight into the solvation process. As such, a purely theoretical method, capable of achieving similar levels of accuracy at an appropriate computational cost, would be a powerful research and development tool.

We have produced several methods utilizing computational chemistry and cheminformatics. Our initial work showed promising theoretical predictions for a set of 25 drug-like compounds. [1] We made predictions via periodic lattice simulation using DMACRYS, and the 3D reference interaction site model with the universal correction. The method produces a correlation coefficient R^2 0.72 and RMSE=1.45 logS units when compared to experiment. These results show a significant improvement compared to the use of continuum solvent methods, using an otherwise corresponding model, for solubility prediction.



Following from this work, we have created a hybrid QSPR methodology that uses traditional 2D descriptors in addition to *ab initio* energies, in order to make a prediction of solubility. This work produced very promising results for a 100-molecule dataset; RMSE 1.11 logS units and R^2 0.59. We reproduced the solubility challenge using this method with RMSE of 0.93 logS units and R^2 of 0.56. [2]

We are currently exploring possible improvements utilising more accurate methodologies for sublimation enthalpy and ultimately free energy prediction. Therefore our attention is now directed to periodic DFT calculations using CASTEP. This work is ongoing; we are using a 48 molecule data set with the PBE exchange and correlation functional and a dispersion corrections. We will additionally seek to produce QSPR methods for sublimation free energy prediction.

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Coarse-Grained Approach for Determining the Self-Assembly of Peptides

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Peptide self assembly has attracted much interest from the food, cosmetic and biomedical industries due to their ability for form large supramolecular networks that are able to form hydrogels. Since there are an infinite numbers of possible peptide combinations, MD simulations are carried out to identify interesting cases.

The computational cost of running these simulations atomistically can be great therefore the MARTINI Coarse Grained approach is used [1]. Coarse Grained Molecular Dynamics is a useful tool in identifying the potential of certain peptides to aggregate.

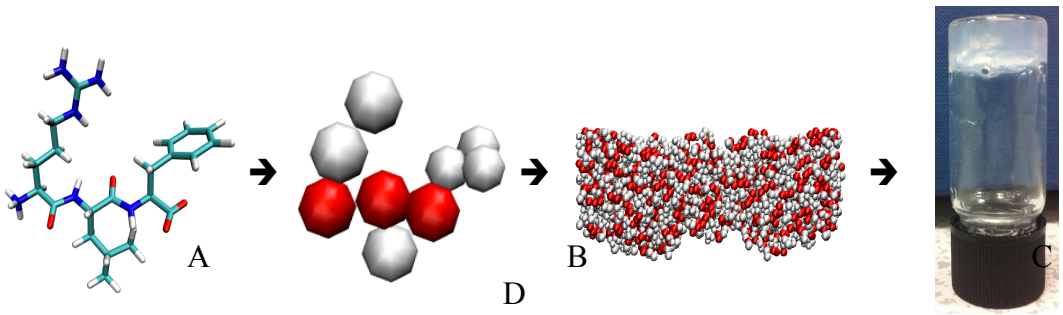

Figure 1: *(A) Atomistic representation of RLF, (B) CG representation, (C) CG MD Simulation , (D) A typical tripeptide hydrogel*

From the simulations it has been seen that the peptides tend to aggregate together into elongated structures, which is typically seen as fibre formation. This shows that it can be used as an important tool for the determining of peptide self assembly.

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Investigation of Non-Additivity in Protein-Ligand Binding

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The design of new drug-like small molecules that bind to a disease-involved protein with high affinity and specificity is a crucial goal in pre-clinical drug discovery. Computational methods that accurately predict free energies of binding could significantly reduce the costs of drug discovery. However, it remains challenging to predict routinely free energies of binding. There are different reasons for this but one of the limiting factors originates from the non-additivity of protein-ligand interactions, i.e. the binding affinity is the sum of numerous enthalpic and entropic contributions that cannot be broken down into functional group contributions and are difficult to quantify using only static structural models of protein-ligand complexes.[(1)]

In principle molecular simulations methodologies that compute free energies of binding can capture non-additivity in protein-ligand binding, but improved analysis and sampling algorithms are necessary to compute well-converged free energies of binding and rationalize subtle non-additive effects. To address these issues, we are investigating with different molecular simulation protocols non-additive effects in series of congeneric Thrombin inhibitors[(2)] by alchemical calculations of their relative free energies of binding. The simulations have been accelerated using the latest Graphics Processing Unit technology by extending the molecular modeling software Sire[(3)] via the OpenMM[(4)] API. A comparison between experimental and predicted relative free energy of binding will be presented.

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Computational Studies of Self-Assembled Monolayers

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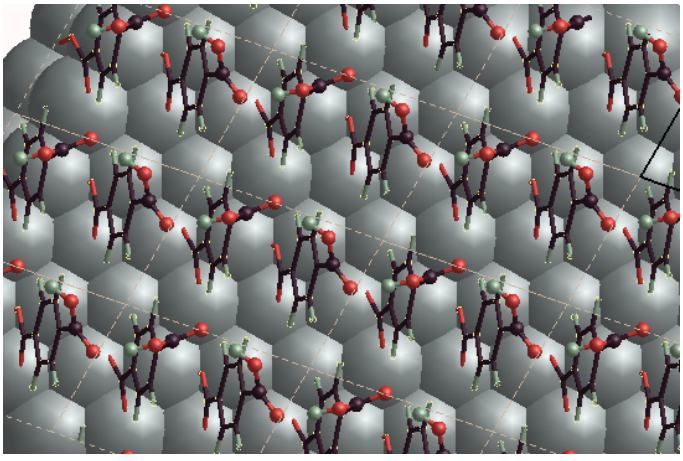
This theoretical study was designed to provide support for endeavours by the group of M. Buck (St Andrews) to elucidate the geometries and physical properties of aromatic carboxylic acids on a double layer of silver on a gold bulk. Our study included gas phase optimisations of the organic molecules using M06-2X/6-31+G* and gas phase geometric scans using the same methods and additionally the PBE/6-31+G* method. However, the majority of this study has focussed on investigating the organometallic systems themselves (with the carboxyl head group proton removed) using periodic calculations (PBE/plane wave, k-point density varied by system, energy cut-off 500 eV). The organometallic systems that were investigated were: biphenyl dicarboxylic acid, biphenyl monocarboxylic acid, the monophenyl analogues thereof, analogues of the dicarboxylic acids with the tail group carboxyl proton replaced by a lithium species, and a system comprising guanine molecules above the biphenyl dicarboxylic acid species. In all cases the organic species were adsorbed onto the (111) surface of a close packed double layer of silver atoms on gold bulk. Despite some limitations on the efficacy of the methods that were computationally feasible, the following conclusions could be drawn. The dicarboxylic acid systems adopted a hydrogen bonding network along the longitudinal dimension of the unit cell. For adsorption, it was found that for the oxygen atoms, top sites and bridge sites were preferred over hollow sites; the potential energy surface is probably quite flat with respect to adsorption site, and the lithium substituted dicarboxylic acids existed as an ionic monolayer (lithium cations). In the calculations that involved guanine molecules it was found that half the guanine molecules formed hydrogen bonds to the biphenyl dicarboxylic acids. However, a more thorough study of possible geometries would be desirable to confirm this finding. The monophenyl systems were found to behave very similarly to their biphenyl analogues.



Optimised structure of biphenyl dicarboxylic acid on silver surface

Protein Druggability: the JEDI Approach

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Several scoring functions have been developed over the last decade to evaluate the druggability -or ligandability- of a protein structure. The majority of existing methods, such as Fpocket, were designed to assess the druggability of crystallographic structures and were not developed to be tightly coupled to molecular dynamics (MD) simulations, in spite of the fact that post-processing of MD trajectories is possible.[1] We present JEDI, a novel computational approach for druggability assessment using a combination of empirical descriptors that can be collected "on-the-fly" during MD simulations.

The Druggable Cavity Directory (http://fpocket.sourceforge.net/dcd) was used to build a data set of 64 diverse proteins in order to parameterize the JEDI scoring function. JEDI is a grid-based approach able to perform the druggability assessment of a binding site in only a few seconds making it one of the fastest methodologies in the field. Agreement between computed and experimental druggability estimates is comparable to literature alternatives. In addition, our estimator is less sensitive than existing methodologies to small structural rearrangements and gives consistent druggability predictions for similar structures of the same protein.

To facilitate evaluation of the druggability of a target at each step of a MD simulation, the JEDI scoring function has been integrated within the PLUMED free energy plugin that supports a broad range of MD packages.[2] Preliminary results show that druggability estimates can be computed for each step of a MD simulation with modest overheads. A unique feature of the approach is that because our druggability function is sufficiently rapid and continuously differentiable, it is possible to: 1) supplement typical potential energy functions with a druggability potential, and 2) exploit information provided by the druggability force to bias molecular dynamics simulations with a variety of free energy methods. Progress towards the identification of cryptic druggable conformations in a range of systems will be reported.

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Geometries, Energies and NMR Parameters of Fluorocyclohexanes from X-ray Crystallography and QM/MM Calculations

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Fluorine chemistry has gained special attention, since fluorine atoms may influence the conformational preferences and, hence, the chemical and biological properties of its non-fluorinated analogues.[1] Indeed, fluorine atoms provide unique molecular properties, which have been explored in all chemistry areas with emphasis in medicinal and material sciences.[2] In particular, Durie *et al*. have reported the synthesis and structure of the *all-syn*-tetrafluorocyclohexanes,[3,4] which may be used as motifs for new liquid crystal materials, since these compounds show two important characteristics: high polarity and low viscosity. However, neither the crystal structure nor the obtained experimental NMR parameters were fully understood yet for these compounds. The present work aims to highlight the experimental observations for the *all-syn*-1,2,4,5-tetrafluoro-3-phenyl-cyclohexane (Figure 1a) using the QM/MM protocol developed by Björnsson and Bühl.[5] In this protocol, the BP86, B3LYP, revPBE and PW6B95 functionals with and without Grimme dispersion corrections were tested. The B3LYP/def2-TZVP theoretical level performs surprisingly well in reproducing the structure in the solid. The theoretically obtained ^{1}H NMR chemical shifts are in good agreement with the experimentally determined values of the analogous *all-syn*-1,2,4,5-tetrafluorocyclohexane (Figure 1b) in toluene solution. Thus, the intermolecular interactions between the phenyl and cyclohexane residues in the solid are indicated to mimic solvation by an aromatic solvent reasonably well.

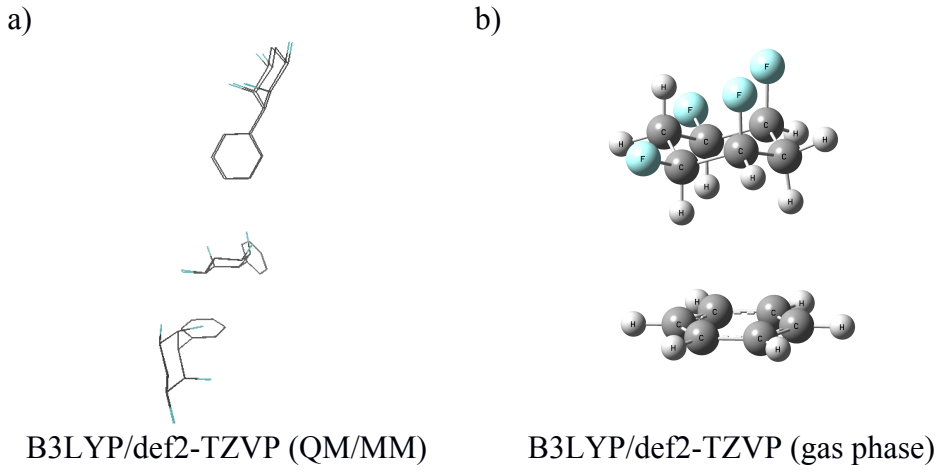

Figure 1: a) Overlay of QM/MM B3LYP/def2-TZVP optimised *all-syn*-1,2,4,5-tetrafluoro-3-phenyl-cyclohexane and the experimental structure in the solid (the trimeric unit used as QM region is shown). b) B3LYP/def2-TZVP optimised complex between *all-syn*-1,2,4,5-tetrafluorocyclohexane and one benzene molecule in the gas-phase.

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Formation of Bioinirganic Complexes by Corrosive Adsorption of (s)-Proline on Ni/Au(111) Surfaces

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The etching of nickel by chiral carboxylic or amino acids is an important consideration in the preparation of chirally modified Ni catalysts for enantioselective hydrogenation reactions[1]. We have investigated the adsorption of (S)-proline onto 2D Ni nanoclusters grown at the elbows of the herringbone reconstruction of the Au{111} surface[2]. X-ray photoelectron spectroscopy (XPS) reveals that the adsorption of proline causes oxidation of the Ni particles. Scanning tunnelling microscopy (STM) shows that the Ni particles decrease in size and ordered molecular arrays are observed to form. The nature of the ordered structures is dependent on thermal treatment, initial Ni coverage and (S)-proline exposure. The fundamental building block of the majority phase observed is a trimeric unit, which we conclude consists of a nickel (III) prolinate unit via analysis of a combination of XPS and high resolution electron energy loss spectroscopy (HREELS). Several of the phases exhibited well defined nano-sized pores which have potential for use as docking sites for prochiral reagents which may have important implications in the design of novel enantioselective heterogeneous catalysts.

DFT calculations confirm that the fundamental building block of the surface structures is indeed an Ni(Proline3) trimer that arranges in different superstructures.

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