<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Achieving Novel Selectivities For Old Reactions Through Catalyst Development</td>
<td>Dr Zhao Yu, Department of Chemistry</td>
</tr>
<tr>
<td>03</td>
<td>Coordinate-Independent Sparse Sufficient Dimension Reduction and Variable Selection</td>
<td>Dr Chen Xin, Department of Statistics &amp; Applied Probability</td>
</tr>
<tr>
<td>05</td>
<td>An Exposure Classification Algorithm for ‘Certainty-Response’ Evaluation in Interview-Based Drug Safety Studies</td>
<td>Dr Yau Wai Ping, Department of Pharmacy</td>
</tr>
<tr>
<td>08</td>
<td>Towards Morse-Kirwan theory on singular spaces</td>
<td>Dr Graeme Wilkin, Department of Mathematics</td>
</tr>
<tr>
<td>10</td>
<td>A Chemical Route to Graphene-based Functional Materials</td>
<td>Dr Goki Eda, Department of Physics, Department of Chemistry</td>
</tr>
<tr>
<td>13</td>
<td>Adding social insects to the DBS environmental mix</td>
<td>Assoc Prof. Theodore Evans, Department of Biological Science</td>
</tr>
</tbody>
</table>

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Faculty of Science research Newsletter is a publication of National University of Singapore.
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Research interests

• Catalyst and methodology development
• Organic and organometallic synthesis
• Medicinal chemistry
• Material science

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Achieving Novel Selectivities For Old Reactions Through Catalyst Development

Dr Zhao Yu
Department of Chemistry

Catalytic Asymmetric Silylation of Alcohols

The chemical syntheses of a variety of biologically active entities including prostaglandins and nucleotides rely on 1,3-cyclopentendiol mono-silyl ether 3 (Scheme 1) as a key chiral building block. Almost all previous preparation of 3, however, utilized the well-established enzymatic deacylation to generate the corresponding enantiopure acetate 2 followed by a lengthy protection-deprotection sequence, since the acyl group in 2 is not compatible with later steps in the syntheses of the natural products. In contrast, silyl ethers have been recognized as one of the best protected forms of alcohols and efficient Lewis base-promoted silyl protection of alcohols has been widely used in chemical synthesis for decades.

A catalytic asymmetric silylation of commercially available 1 would provide a one-step procedure (instead of 6 steps) to prepare 3 and thus significantly increase the efficiency with which those biologically active entities can be synthesized. Such a process was never reported, to our surprise, partially due to the fact that there is no biological blueprint available for asymmetric silylation of alcohols.

Through careful catalyst design and extensive catalyst screening, we were able to identify amino acid-based N-methylimidazole 4 as a highly enantioselective catalyst for the silylation of a variety of 1,3- and 1,2-diols and with various silylating reagents (Scheme 2). The desired mono-silyl ether products were obtained in high chemical yields with excellent enantioselectivities (ee: enantiomeric excess). The catalyst is believed to serve bifunctional activation of the silylating reagent (by forming a hypervalent silicate) as well as the diol (by H-bond interaction and general base catalysis), as illustrated by the proposed transition state model (in brackets). The reactions are operationally simple. The catalyst can be easily prepared and is now commercially available from Aldrich.
The catalytic asymmetric silylation of alcohols was extended to kinetic resolution of racemic 1,2-diols and desymmetrization of meso-triols, including the application to the total synthesis of cleroindicin D (Scheme 3).\(^7\)

In spite of impressive advances in the development of catalytic olefin metathesis reactions,\(^9\) lack of stereoselective access to \(Z\)-alkenes represented a significant shortcoming in olefin metathesis for decades. It is difficult to come up with a catalytic system that delivers \(Z\)-alkenes kinetically; isomerization of \(Z\)-alkenes to the lower-in-energy \(E\)-alkenes further complicates the situation since most metathesis reactions are under thermodynamic control.

Based on the discovery and development of novel Mo-alkylidene complexes,\(^9\) and the \(Z\)-selective ring-opening cross metathesis reactions (which are irreversible reactions due to release of ring strain in the substrates),\(^10\) we developed the first \(Z\)-selective metathesis homocoupling of terminal olefins to access disubstituted olefins with good to excellent levels of \(Z\)-selectivity (Scheme 4).\(^11\) The isomerization pathway was minimized by the use of the less reactive \(W\)-complexes such as \(5\) supported by the sterically bulky 3,3’-bismesityl-aryloxide, resulting in a better conservation of the kinetic \(Z\)-selectivity.

An intriguing model for the \(Z\)-selectivity was proposed: in the trigonal bipyramidal metallacyclobutane intermediate, the combination of a sterically demanding but freely rotating (around the Mo-O bond) aryloxide and a sufficiently smaller imido group favors reaction through the syn alkylidene isomer and the approach of the incoming alkene with the substituents directed towards the imido ligand to form an all-cis metallacyclobutane. Cycloreversion then produces \(Z\)-alkene products with regeneration of the syn alkylidene.

**References:**

Dr Chen Xin joined Department of Statistics & Applied Probability, National University of Singapore on June 2011 as an assistant professor. He graduated from NUS with a master degree in 2003. After working in Singapore for a while, he moved to US in 2005 and got his Ph.D from University of Minnesota in 2010. He had worked as an assistant professor in Mathematics Department at Syracuse University for one year.

Research in his group currently includes:
- Dimension Reduction
- Variable Selection
- Statistical Computing
- Bioinformatics

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Coordinate-Independent Sparse Sufficient Dimension Reduction and Variable Selection

Dr Chen Xin
Department of Statistics & Applied Probability

Introduction

Sufficient dimension reduction (SDR) in regression, which reduces the dimension by replacing original predictors with minimal set of their linear combinations without loss of information, is very helpful when the number of predictors is large. The standard SDR methods suffer because the estimated linear combinations usually consist of all original predictors, making it difficult to interpret. In this paper, we propose a unified method – coordinate-independent sparse estimation (CISE) – that can simultaneously achieve sparse sufficient dimension reduction and screen out irrelevant and redundant variables efficiently.

Consider the regression of a univariate response $y$ on random predictor vector $x=(x_1,…,x_p)$, with the general goal of inferring about the conditional distribution of $y$ given $x$. When $p$ is large, most statistical methods face the “curse of dimensionality”, and thus dimension reduction is desirable. Sufficient dimension reduction (SDR) introduced by Cook [1] is important in both theory and practice. It strives to reduce the dimension of $x$ by replacing it with a minimal set of linear combinations of $x$, without loss of information on the conditional distribution of $y$ given $x$. The central subspace $S$, which is the intersection of all dimension reduction spaces, is an essential concept of SDR and the parameter of interest. The dimension $d$ of $S$, usually far less than $p$, is assumed to be known in this article.

There has been considerable interest in dimension reduction methods since the introduction of sliced inverse regression (SIR) [2] and sliced average variance estimation (SAVE) [3]. Recently, Li and Wang [4] proposed directional regression (DR). In contrast to these and other moment-based SDR approaches, Cook [5] introduced a likelihood-based paradigm for SDR that requires a model for the inverse regression of $x$ on $y$. This paradigm, which is broadly referred to as principal fitted components (PFC), was developed further by Cook and Forzani [6]. Likelihood-based SDR inherits properties and methods from general likelihood theory and can be very efficient in estimating the central subspace.

All of the aforementioned dimension reduction methods suffer because the estimated linear reductions usually involve all of the original predictors $x$. As a consequence, the results can be hard to interpret, the important variables may be difficult to identify and the efficiency gain may be less than that possible with variable selection. These limitations can be overcome by screening irrelevant and redundant predictors while still estimating a few linear combinations of the active predictors. Some attempts have been made to address this problem in dimension reduction generally and SDR in particular. For example, L. Li et al. [7] proposed a model-free variable selection method based on SDR. Zou et al. [8] proposed a sparse principal component analysis. Ni et al. [9] introduced a shrinkage version of SIR.

However, most existing sparse dimension reduction methods are conducted stepwise, estimating a sparse solution for a basis matrix of the central subspace column by column. Instead, in this article, we propose a unified one-step approach to reduce the number of variables appearing in the estimate of $S$. Our approach, which hinges operationally on Grassmann manifold optimization, is able to achieve dimension reduction and variable selection simultaneously. Additionally, our proposed method has the oracle property: under mild conditions the proposed estimator would perform asymptotically as well as if the true irrelevant predictors were known.
Our method starts from generalized eigenvalue problems. Many moments based sufficient dimension reduction methods can be formulated as a generalized eigenvalue problem. Incorporated with a so-called coordinate-independent penalty function and Bayesian information criterion to select the tuning parameter in the penalty function, we reach our coordinate-independent sparse estimation (CISE). To overcome the non-differentiability of the penalty function, we adopt the local quadratic approximation of Fan and Li [10]; that is, we approximate the penalty function locally with a quadratic function at every step of the iteration. The algorithm is quite fast, usually requiring a few dozen iterations. Simulation studies and a real-data example demonstrate the effectiveness and efficiency of the proposed approach.

References
An Exposure Classification Algorithm for ‘Certainty-Response’ Evaluation in Interview-Based Drug Safety Studies

Dr Yau Wai Ping
Department of Pharmacy

Introduction

In pharmacoepidemiology, interview data provide a valuable source of exposure information for studies that are focused on actual use of medications (rather than on evidence of prescription or dispensing). However, given that exposure information often is obtained retrospectively in interview-based studies, the precise ascertainment and classification of medication use may be limited by imperfect recall of exposure timing. Although some subjects may be able to recall exact start and stop dates, others may only be able to recall a more imprecise time frame (e.g., sometime in particular month(s)). This is an important consideration in studies where accurate timing of exposure is critical, such as etiologic studies of birth defects, where gestational timing of exposure is crucial. Consider two scenarios: Ms. Smith and Ms. Jones have the same dates for their first trimesters, from mid-February to mid-May 2010. Ms. Smith is able to specifically recall her medication use of seven days starting on May 1 and stopping on May 7. We can be relatively confident that, based on this report, Ms. Smith was exposed in the first trimester. Alternatively, Ms. Jones is not able to recall the exact dates of exposure but only that she took the medication for seven days, starting and stopping sometime in May 2010. We can only say that Ms. Jones was possibly exposed in the first trimester.

In most etiologic studies, study subjects are usually dichotomized into exposed or unexposed for the period of interest. However, questionnaires may collect exposure details including the dates when exposure began and ended, the interviewee’s estimates of the certainty of recall of each of these dates (e.g., exact date or more imprecise time frame), and the duration of exposure; such information can allow drug exposure to be classified according to certainty of use during a given time window. This more detailed classification allows evaluation of ‘certainty-responses’ (stronger association with higher level of certainty), which, like dose-responses, would, if demonstrated, support a true association between the exposure and outcome under study.

Algorithm to classify timing of exposure

Using detailed prenatal medication exposure information collected retrospectively through maternal interviews as part of the Slone Epidemiology Center Birth Defects Study, we developed an exposure classification algorithm, taking into account recall certainty in reported timing of medication exposure.

We considered exposure in the first trimester (encompassing the etiologically important period of structural development for most organ systems) to include maternal use of medication on at least one day during that period. Based on the precision of the start and stop dates reported by the subjects and duration of use, we classified drug exposure into four categories: (i) completely unexposed during pregnancy; (ii) likely exposed in the first trimester of pregnancy; (iii) possibly exposed in the first trimester; and (iv) exposed outside the first trimester. For uncertain start/stop dates reported as being sometime in a particular month, we considered the possible exposure period to be the widest interval consistent with her report (e.g., if a mother reported medication use starting and stopping in May, we assigned May 1 as her start date and May 31 as her stop date). We classified a mother...
as being likely exposed in the first trimester if her medication use, given her duration of use but independent of date certainty, had to at least partially include the first trimester. She was classified as possibly exposed if the use, given the reported duration but based on uncertain dates, could fall within the first trimester or completely outside of it. Figure 1 depicts all possible exposure scenarios in relation to the window of interest and provides the drug exposure classification, as well as some case examples, for each scenario.

**Application of exposure classification algorithm**

We applied the algorithm to study an association between prenatal tetracycline exposure and risk of congenital heart defects previously reported by the National Birth Defects Prevention Study,\(^1\) using 1993–2008 data from 11,517 subjects in the Slone Epidemiology Center Birth Defects Study. Compared with non-use of systemic tetracyclines during pregnancy, the odds ratio (OR) for exposure outside the first trimester was 1.0 (95% confidence interval (CI) 0.4–2.5), and that for exposed (likely or possibly, combined) in the first trimester was 1.7 (95% CI 0.9–3.2); however, the ORs based on the more detailed classification of first-trimester exposures derived from the algorithm were 0.9 (95% CI 0.3–3.0) for possibly exposed and 2.2 (95% CI 1.0–4.6) for likely exposed. A ‘certainty-response’ (stronger association with higher level of certainty) was found with our classification of exposure into “possibly exposed” and “likely exposed” in the window of etiological interest, which, in this case, was the first trimester. These findings suggest that an algorithm based on ‘certainty-responses’ may have value in increasing the accuracy of exposure classification.

This approach of ‘certainty-response’ algorithms can be extrapolated to other epidemiologic studies where accurate timing of exposure is crucial and where data sources have available detailed exposure information that facilitates consideration of the certainty of exposure timing. The use of ‘certainty-responses’ may provide more valid risk estimates for the exposure-disease relation and thereby enhance the identification of true associations.

Although we focused on medication use as our exposure, the algorithm can be applied to classify any exposure (e.g., cigarette smoking, alcohol consumption, and infection). The algorithm may have its greatest value for exposures with short durations relative to the window of interest (including exposures at irregular intervals such as medications used on an “as needed” basis), where uncertainty in exposure timing may be more of an issue. This was the case in our example of antibiotics, with an average duration of 12 days and an exposure window of one trimester. Clearly, the shorter the duration of exposure and the narrower the critical window, the more challenging it will be to classify timing of exposure accurately. For exposures with long durations (e.g., chronically taken medications like anti-hypertensives and anti-diabetics), uncertainty in exposure timing would be of less concern, and the algorithm would have little added value.

In conclusion, algorithms for exposure classification that incorporate the subject’s self-reported certainty regarding exposure dates may be useful in interview-based drug safety studies, particularly for exposures of short duration.

**References:**

Figure 1. All possible exposure scenarios in relation to the window of interest and the respective exposure classification for each scenario. The white rectangle depicts the window of interest, with the boundaries denoting the start and stop dates, respectively, that define an exposure within that window. The horizontal arrows identify the possible exposure period, with the left and right arrow heads denoting the start and stop dates of exposure, respectively. The shaded bars depict the duration of exposure.

Table:

<table>
<thead>
<tr>
<th>Exposure Scenarios</th>
<th>Exposure Classification For Each Scenario</th>
<th>Case Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Window of interest (e.g., first trimester of pregnancy)</td>
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<tr>
<td>Scenario 1: Exposure period occurs exclusively within window of interest</td>
<td>“Likely exposed in window of interest”</td>
<td>E.g., Use of Medication A is reported as starting from March 1, 2010 and stopping on March 14, 2010</td>
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<tr>
<td>Scenario 2: Exposure period occurs exclusively outside window of interest, either</td>
<td>“Exposed outside window of interest”</td>
<td>E.g., Use of Medication B is reported as starting from January 30, 2010 and stopping on February 6, 2010</td>
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<td>• exposure period starts and ends before window of interest, or</td>
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<td>E.g., Use of Medication C is reported as starting from June 30, 2010 and stopping on July 30, 2010</td>
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<td>• exposure period starts and ends after window of interest</td>
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<td>Scenario 3: Exposure period occurs both within and outside window of interest, either</td>
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<td>• exposure period starts before and ends within window of interest, or</td>
<td>(a) If duration of use at least partially overlaps window of interest: “Likely exposed in window of interest”</td>
<td>E.g., Use of Medication X is reported as starting sometime in January, 2010 (we assigned January 1, 2010 as the start date) and stopping sometime in April, 2010 (we assigned April 1, 2010 as the stop date), and (a) duration of use of 60 days, or (b) duration of use of 30 days, or unknown duration of use</td>
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<td>(b)</td>
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<tr>
<td>• exposure period starts within and ends after window of interest, or</td>
<td>(a)</td>
<td>E.g., Use of Medication Y is reported as starting sometime in March, 2010 (we assigned March 1, 2010 as the start date) and stopping sometime in July, 2010 (we assigned July 1, 2010 as the stop date), and (a) duration of use of 90 days, or (b) duration of use of 7 days, or unknown duration of use</td>
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<td></td>
<td>(b)</td>
<td></td>
</tr>
<tr>
<td>• exposure period starts before and ends after window of interest</td>
<td>(a)</td>
<td>E.g., Use of Medication Z is reported as starting sometime in December, 2009 (we assigned December 1, 2009 as the start date) and stopping sometime in June, 2010 (we assigned June 30, 2010 as the stop date), and (a) duration of use of 90 days, or (b) duration of use of 14 days, or unknown duration of use</td>
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<td>(b)</td>
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Towards Morse-Kirwan theory on singular spaces

Dr Graeme Wilkin
Department of Mathematics

Morse Theory

Morse theory was originally developed in the 1920s by Marston Morse to study geodesics on a sphere. Since then it has undergone a number of improvements and generalisations in order to study different types of problems; for example Smale's proof of the Poincare conjecture in higher dimensions, Milnor's construction of exotic differentiable structures on spheres and Kirwan's method for computing the cohomology of symplectic and algebraic quotients.

A special case of the original problem studied by Morse is easy to visualise. Start with a standard two-dimensional sphere (for example, the surface of the earth). The shortest path between two points on the sphere runs along a segment of a great circle. These shortest paths are called geodesics. For example, two cities with the same longitude will be connected by a great circle that runs north-south, and two cities on the equator will be connected by a geodesic that runs along the equator. Any other circle of constant latitude is not a geodesic.

Also of interest are the closed geodesics, i.e. those that form a closed loop on the sphere rather than a path between two distinct points. For example, the equator and circles of constant longitude are closed geodesics.

Sometimes the notion of "shortest path" needs to be redefined to suit the application at hand. For example, an airplane would like to travel along the shortest path in order to save fuel, however factors such as prevailing winds or the recent volcanic eruption in Iceland may mean that it is more efficient to travel along a slightly different path. Mathematically, this change in perspective to looking for the most efficient path instead of the shortest path is expressed as a change in the metric, or distance measure on the sphere. One of the questions that Morse answered was: Given a smooth metric on the two-sphere, are there non-trivial closed geodesics?

The metric associates a real number (the length) to each loop on the sphere, and Morse's approach to this question was to consider the length function on the space of all loops on the sphere. The minimum corresponds to the set of trivial loops (a trivial loop is just a single point on the sphere), the non-minimal critical points correspond to the non-trivial closed geodesics, and Morse theory relates the topology of the total space (the space of all loops) to the topology of the critical sets. After developing the mathematical machinery to do this, Morse's theorem that nontrivial closed geodesics exist is then just the observation that the topology of the total space is different to the topology of the minimum (and therefore non-minimal critical points must exist).

Morse theory and the Yang-Mills equations

Physical systems naturally tend towards a minimum energy configuration, and Morse theory can sometimes provide a convenient tool for studying the topology of the space of minimum energy solutions. A famous example of this is contained in the work of Atiyah and Bott [1], who used the Morse theory of the Yang-Mills functional to study the topology of the space of solutions to the Yang-Mills equations in two dimensions. The physical relevance of the Yang-Mills equations is in four dimensions; for example they play a key role in the Nobel prize-winning work of Salam, Glashow and Weinberg. In the two-dimensional case, rather than constructing a single solution and studying its properties, the goal is instead to understand the topology of the total space of solutions that lie at the minimum of the Yang-Mills functional (the "energy" function).
One would also like to extend Atiyah and Bott's theory to study related equations that are also physically relevant and of geometric interest. Two such equations are the two-dimensional Yang-Mills-Higgs equations and the equations defining a Nakajima quiver variety (which were introduced to parametrise Yang-Mills instantons over gravitational instantons). The Yang-Mills-Higgs equations were originally developed in the study of Higgs coupling, and the two-dimensional equations have found applications in mathematical fields such as geometric structures on surfaces, integrable systems and the proof of the fundamental lemma in the Geometric Langlands program. Topological information about Nakajima quiver varieties has been used to construct representations of quantum algebras [2], which (among other applications) have been used in the study of the statistical mechanics of lattice models, such as the Ising model of a magnet [3].

The obstruction to using Atiyah and Bott's methods to study quiver varieties and the Yang-Mills-Higgs equations is that now the total space is singular, and a priori no theory exists for the Morse theory of these energy functionals. Together with collaborators we have been able to overcome these difficulties to produce new results about the topology of the space of solutions to the Yang-Mills-Higgs equations in low rank [4], [5]. The analogous program for quiver varieties leads to many interesting conjectures and questions, such as whether these techniques will shed new light on representations of quantum algebras and the mathematics of solvable lattice models.

References:

A Chemical Route to Graphene-based Functional Materials

Dr Goki Eda
Department of Physics
Department of Chemistry

Introduction

Discovery of graphene, a single atomic sheet of sp² carbon, has sparked intense research activities during the past few years. This truly two-dimensional allotrope of carbon, increasingly recognized for its superior properties including record strength, impermeability of any molecules, unusually high carrier mobility, and exceptionally large conductivity of heat and electricity, continues to attract and fascinate researchers from different scientific disciplines¹. While the initial observation of ambipolar field effect and high carrier mobility triggered tremendous interest in its application in nano-electronics, other intriguing features of graphene demonstrate its potential in photonics, molecular sensing, energy storage, medical diagnostics, and composites to name a few.

In order to realize the technological potential of graphene, manufacturing challenges such as scalable synthesis, uniform deposition, and integration into realistic device structures must be addressed. Importantly, graphene manufacturing must be compatible with industrial processes and scalable at a reasonable cost. Graphene can be produced in a number of ways in the laboratory scale but very few of these are suitable for large-scale continuous production. Discovery and widespread popularity of graphene were facilitated by the well-known “Scotch tape method” where a piece of graphite crystal is mechanically cleaved down to a single monolayer². This method yields high quality graphene which exhibits exotic condensed matter phenomena but the deposition is not controllable and limited to a small area. The last couple of years have seen significant progress in large-area chemical vapour deposition where graphene is grown on copper surface from a carbon source such as methane and subsequently transferred to a desired substrate³. However, there is still a significant challenge in scaling up the processes and meeting the industrial throughput requirements.

Graphene can also be produced in mass quantity via exfoliation of graphite in solution⁴, ⁵. This can be achieved via various methods and results in a colloidal suspension of micron-sized graphene flakes. Since graphite is an inexpensive and ubiquitous resource, this approach to large-scale production of graphene holds tremendous promise. Theoretically, a few grams of any molecules, unusually high carrier mobility, and exceptionally large conductivity of heat and electricity, continues to attract and fascinate researchers from different scientific disciplines¹. While the initial observation of ambipolar field effect and high carrier mobility triggered tremendous interest in its application in nano-electronics, other intriguing features of graphene demonstrate its potential in photonics, molecular sensing, energy storage, medical diagnostics, and composites to name a few.

Graphene oxide

It has been known over 150 years that oxidation of graphite can be achieved by placing it in one or more concentrates acids in the presence of an oxidizing agent⁶. The resulting material, graphite oxide, is hydrophilic in contrast to graphite and dissolves readily in water. It was only recently recognized that upon hydrolysis graphite oxide exfoliates into individual monolayers⁷. These monolayers, called graphene oxide, consist of a graphene sheet decorated with oxygen-containing functional groups (Figure 1). The basal plane of GO is partially covered by hydroxyl and epoxide groups while the edges are terminated with carboxyl, carbonyl and a host of other groups⁸. The covalent bonding of oxygen strongly modifies the electronic properties of graphene making it an electrical insulator. GO is often considered as a precursor to graphene because it can be reduced to obtain a graphene-like material with similar electrical conductivity.

Due to ionization of the edge groups, GO can be electrostatically stabilized in water, forming a colloidal suspension⁹. Solubility of GO allows its deposition into thin film structures using conventional techniques such as spin-coating. Although individual sheets of GO are microscopic in size (typically 1 ~ 100 μm), they can be spread over a substrate forming a continuous macroscopic film like a “quilt patchwork”. The deposition conditions can be carefully tuned to produce ultra-thin films with thicknesses ranging from a single monolayer to tens of layers⁹. Subsequent reduction leads to formation of an electrically conductive,
highly transparent and flexible material (Figure 2). Thus, in a few simple steps, raw graphite powders can be transformed into a material which realizes the attractive attributes of graphene in macroscale. Studies have revealed the unique and sometimes unexpected properties of reduced GO thin films, providing prospects for their use as transparent conductors, chemical/biological sensors, thin-film transistors, electrodes, ultracapacitors, field emitters, photovoltaics, photo-detectors, nanoelectromechanical resonators, and nonvolatile memory devices.

**Tailored chemistry**

Graphene oxide is chemically heterogeneous and its chemical composition can be continuously and reversibly tuned through oxidation and reduction. Because covalent oxygen bonding alters the orbital hybridization of carbon in graphene, the electronic structure of GO strongly depends on the oxygen coverage. As-synthesized GO exhibits oxygen coverage of around 60% and the rest of the carbon atoms remain sp² hybridized. Interestingly, the sp² phase exists in clusters surrounded by heavily oxidized regions predominantly consisting of sp³ carbon. The size of these sp² clusters were found to be approximately 2 ~ 3 nm in size. While confinement of π electrons inside these clusters inhibits electrical conduction, conductive pathways form as the material is reduced. Typically, reduction of GO leads to increase in conductivity by ~ 6 orders of magnitude. The dramatic change in conductivity reflects substantial evolution of electronic structure from finite gap insulator to graphene-like semimetal. When GO is only partially reduced, it exhibits semiconducting behaviour where electrostatic modulation of conductance with distinct off-state can be achieved. These observations indicate that oxidation and reduction can be used as a knob to tune the electronic structure of GO over a wide range.

Structural inhomogeneity is a unique attribute of GO. Electronically, it can be viewed as a hybrid of conductive sp² and insulating sp³ phases. In other words, GO represents a two-dimensional platform on which molecule-like sp² domains are embedded. Remarkable consequence of this unique structure is the photoluminescence properties. This is in striking contrast to graphene where emission of light is inhibited due to lack of energy gap. Experiments have shown that depending on oxidation and reduction, GO exhibits photoluminescence with different energies across the visible spectrum. Currently, tunability of the emission wavelength and the quantum yield are not impressive, probably owing to defects and disorder. Nevertheless, it is expected that careful control of functionalization will be key to achieving defined electronic structure and thus truly tuneable and efficient emission.

**Outlook**

As intense research continues, technological significance of graphene is increasingly recognized. In order to implement practical applications, a scalable route to synthesis needs to be realized. Chemical exfoliation of graphite provides a practical solution to low-cost bulk production and ease of deposition of graphene-based thin films. Chemical versatility of GO is a unique feature of the material that allows dispersion in liquids, integration with other materials, and tailoring of its optical and electrical properties, providing prospects for previously unpredicted applications such as drug delivery and cellular imaging. Although the structure of GO plays a critical role in the physical properties, its precise control is currently lacking. Therefore chemists from various backgrounds will be needed to tackle this issue. Graphene oxide with distinct chemical and atomic structure will offer an exciting platform to explore fundamental science as well as a practical route to applications.

**Figure 1**
Schematic illustration showing tuneable chemical structure of graphene oxide. Inset shows a photograph of colloidal suspensions of graphene oxide (left) and partially oxidized graphene (right).
Figure 2
A 12 inch diameter ultra-thin film of reduced graphene oxide on a PET substrate. Inset shows deposition of graphene oxide on a 12 inch silicon wafer. (Photographs by courtesy of Dr. Hisato Yamaguchi)

References:
Adding social insects to the DBS environmental mix

Assoc Prof. Theodore Evans
Department of Biological Science

Research article

A/P Evans has worked on a variety of topics; most have focussed on social insects in particular, or used social insects as models systems, or for their effects in their communities. Sociality is relatively rare among animals and has immediate negative consequences, compared with solitary animals. Charles Darwin described the sterile worker caste found in social insects as his ‘special difficulty’ in his seminal work Origin of Species, and as such it has attracted considerable scientific attention, and the theoretical resolutions of this ‘special difficulty’ has effected all evolutionary theory exemplified in The Selfish Gene by Richard Dawkins. Not only has our understanding of the complexities of the evolution of derived sociality in insects grown over time, so has our realisation that that social insects probably play an important role in ecology and environment. Social insects are very diverse and super abundant; studies indicate that there is greater biomass of ants and termites than vertebrates in some habitats. Large biomass usually means large effects in community ecology. A/P Evans researches the ecological impacts of social insects, in particular ants and termites, in natural and agricultural landscapes.

A/P Evans’ major research areas include:
(1) Organization of cooperative behaviour
(2) Ecosystem services of insects.
(3) Community ecology of ants and termites.
(4) Effects of human activity on ecology and evolution, (i) invasive species; (ii) novel ecosystems.

(1) Organization of cooperative behaviour

Bees, ants and termites are examples of highly eusocial societies, and the populations of these societies can number in the millions. Such societies have co-ordinated, cooperative activities that rely on accurate information gathering and communication. The best known forms of this communication are the complex dances of honeybees, and the diverse mix of pheromones in ants. In contrast, termite communication is poorly understood. A/P Evans has focussed on vibro-acoustic signals in termites; because all termite species use a ‘head-banging’ alarm signal, which was first documented over 300 years ago but little studied since. A/P Evans collaborates with Prof. Joseph Lai of the University of New South Wales in Australia, together they have demonstrated that termites can detect wood size using vibrations generated by their chewing and that different species can be distinguished using vibrations also. His ongoing work investigates further information gained from vibro-acoustic signals, including food and predators.
(2) Ecosystem services of insects

Biodiversity provides critical beneficial ecosystem services, such as water purification, soil health and carbon sequestration, yet the ecosystem function underlying these services is poorly understood as they are regulated by small and prosaic organisms, such as ants and termites. Ants and termites regulate key ecological processes such as decomposition, nitrogen fixation, nutrient cycling, herbivory and seed dispersal, and are widely regarded as ‘ecosystem engineers’. A/P Evans and his colleagues at CSIRO and the University of Sydney tested whether these tiny yet numerous insects can be used to garner ecosystem services in a dryland agricultural system using wheat. They have found ants and termites increase wheat yield by 36%, due to higher water infiltration down their tunnels and improved soil nitrogen. Ants provided significant weed control by consuming 50% of weed seeds. A/P Evans’ future work will consider new crops in different climates.

(3) Community ecology of ants and termites

The eminent Harvard biologist Professor EO Wilson famously stated that ants and termites are “the little things that run the world” in 1986. This influential assertion has never been tested experimentally, until now. A/P Evans with collaborators in CSIRO, Oxford University, Natural History Museum London, and Federal University of Viçosa will run large scale field experiments in savannah in Australia, South Africa and Brazil to quantify the effect ants and termites play in the key ecological processes of decomposition, nutrient cycling, nitrogen fixation, herbivory, seed dispersal, soil structure and water infiltration. They will use recently developed taxa-specific baits, in part developed and tested by A/P Evans as part of his work with industry, to exclude either ants or termites or both taxa. The results are expected not only to shed light on Prof. Wilson’s statement and so extend current knowledge of functional and community ecological theory, but it is hoped it will contribute to land management for conservation and agricultural production.
A/P Evans plans two sub-projects with the larger experiment. The first will examine the community structure of termites. How so many species with essentially the same requirements (i.e. all termites depend fundamentally on cellulose, most wood eating species can consume any species of wood) coexist in the same habitat remains unexplored. Preliminary work suggests that, like ants, termite species have a competitive hierarchy, and that subordinate species avoid dominant ones by eavesdropping on vibro-acoustic signals. The second sub-project will examine the dogma that ants are the most important predators of termites. This dogma is based on little more than anecdotal observations; no empirical evidence exists for ants either limiting or being limited by termite populations.

(4) Effects of human activity on ecology and evolution, (i) invasive species.

Invasive species of plants and animals are well known as economic and ecological pests, increasing costs to various industries and threatening biodiversity. Much work on invasive species concerns these issues and control; understanding the origins of these species and the histories of invasion has received considerably less attention. A/P Evans plans new research on a variety of invasive insect species, both those originating in South East Asia and those introduced to the region. This research will use a variety of molecular markers to investigate population structure. South East Asia is an excellent region for such research, because of the effect of repeated isolation and joining of islands between and during glaciations, and the many centuries of trade that have produced tramp/invasive species elsewhere in the world.

Most ecologists accept that primary forests have the highest biodiversity and provides the highest levels of ecosystem services of any habitat. Primary forests are under increasing threat, due to land use change, primarily the logging or clearing of forested land. This is particularly true in South East Asia and Singapore may represent the end point of land use change, with less than 2% of its original primary forest intact. Yet land once cleared does not remain empty; unmanaged land is colonised by fast-growing native pioneers and ruderal exotics, some of which are invasive, and over time will gain slower growing native species. These unmanaged lands are little studied, with even alpha level biodiversity poorly known. Together with Associate Prof. Hugh Tan also of DBS, A/P Evans is investigating the biodiversity of Singapore's unmanaged 'wasteland' landscapes, plant and invertebrate diversity. Of particular interest from the theoretical ecological perspective is the combination of resulting dynamics of species that did not evolve together. Combinations of indigenous and exotic plants will lead to novel competitive interactions, and native insects will function as pollinators and herbivores of the non-native plants. Once biodiversity is documented, research into function and ecosystem services will commence. Singapore offers a natural field experiment comparing the natural primary rainforests of Bukit Timah with the unmanaged ‘wastelands’. A comparison of the communities living in these habitats will allow insight into whether the novel ecosystems on ‘wasterlands’ can provide significant and useful services to the nation.

A/P Evans with an Amitermes meridionalis mound: as the name suggests, these termites build their mounds parallel with north-south meridions. This unique alignment allows capture of the early morning sun to warm the mound rapidly
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