Joint
Environment and Human Health
Programme

Annual Science Day and Workshops
11th and 12th February 2008

Polaris House
Swindon

Systems Approaches and Complexity Workshop Abstracts

Systems Biology: The Middle-Out approach

Prof Denis Noble

Understanding the logic of living systems requires knowledge of the mechanisms involved at the levels at which functionality is expressed. This information does not reside in the genome, nor even in the individual proteins that genes code for. Functionality emerges as the result of interactions between many proteins relating to each other in multiple cascades and in interaction with the cellular environment. To understand functionality there is therefore no alternative to copying nature and computing these interactions to determine the logic of healthy and diseased states. The rapid growth in biological databases, models of cells, tissues and organs and in computing power has made it possible to explore functionality all the way from the level of genes to whole organs and systems. The approach is neither bottom-up nor top-down. Brenner invented the correct term: middle-out (Noble, 2006). In this lecture I will use models of the heart to demonstrate that this approach enables us to go all the way from individual genetic information (on mutations, for example) to exploring the consequences at a whole organ level.

Developing Multi-Scale Mathematical Models of the Heart

Dr Nic Smith

Predicting information about human physiology and pathophysiology from genomic data is a compelling, but unfulfilled goal of post-genomic biology. This is the aim of integrative multi-scale physiology and is, undeniably, an ambitious goal. Yet if we can exploit even a small proportion of the rich and varied experimental data currently available, significant insights into clinically important aspects of human physiology will follow. To achieve this requires the integration of data from disparate sources into a common framework. Extrapolation of available data across species, laboratory techniques and conditions requires a quantitative approach. Mathematical models allow us to integrate sub-cellular information into cellular, tissue and organ-level, and ultimately clinically relevant scales. In this talk I will use the Heart as an example to argue that biophysically detailed computational modelling provides the essential tool for this process. Recently developed models of cellular contraction and excitation in disease will be presented. The methods of how these cell models are embedded in spatial representations of tissue will then be outlined. Using these tissue models, combined with anatomical and structural information, simulations of whole heart activation, mechanics and coronary blood flow will be demonstrated. Finally the issues associated with developing an appropriate framework for annotating, data basing and critiquing these types of models will be discussed and their importance for the development of integrative computational biology.

Climate Change Impacts on Human Health
Dr Mark McCarthy

Climate change is now widely recognised as a significant challenge for society and the environment in the coming century. Warming of the global climate system during the 20th century is very likely to be a response to man-made greenhouse gas emissions. Continued emissions at or above the current rate are very likely to induce further changes to the climate system, larger than observed so far. Human health can be affected by climatic change both directly through exposure to changes in temperature, precipitation and extreme events, or indirectly though food and water availability or changes to ecosystems and the spread of disease. In this presentation I will outline a number of key issues concerning climate change and human health, and outline ongoing activities aimed at integrating climate impacts assessments directly within physically-based climate change models.

Approaches to Modelling Toxic Reactions in Biological Systems from Organisms to Ecosystems
Icarus Allen

The talk will outline current approaches to modelling environmental health in marine ecosystems at both an organismal and ecosystem level. I will present models of the impacts of toxins on marine molluscs, along with models of whole marine ecosystems. The application of ecosystem models as near real time forecast tools for Harmful Algal Blooms (HABS) will be emphasised. The role of both climatic and anthropogenic drivers on the health of marine ecosystems will be discussed along with the linkage between processes at organismal and ecosystem levels.

Epidemiology: Genetics to the Rescue?
Prof David Melzer

Studies of the effects of environmental toxins in human populations face many challenges. Exposure to specific hazards tends to be correlated with other exposures, so confounding is common and difficult to control. Individual responses to toxins can vary greatly, with part of this variation being inherited.

Recent genome wide association studies have identified many new genetic variants associated with common disease. Some of the findings suggest causal mechanisms: for example, one of the large effect allergy and asthma mutations disrupts a skin protein, suggesting a failed barrier element in allergy. Much has been learned about the gene variants explaining auto-immune conditions. As genotype is assigned randomly at birth, genetic variation sometimes offers natural experiments which illuminate causality.

Much previous work has focussed on toxic effects in the young, but with improving health status in western populations, disease in the young is now relatively uncommon. Opportunities for studying the accumulated effect of toxins on cell damage and the ageing process are emerging. Genetic variation associated with age related disease may provide an opportunity for identifying the common effects of longer term toxic loads.

Meeting the Challenge of Complexity
Prof John Crawford

Complexity is an elusive concept that pervades the physical and mathematical sciences and is making inroads into the life sciences particularly in evolutionary ecology and systems biology. Loosely speaking, we are talking about systems of many strongly interacting parts that exhibit organisation (or emergent behaviour) on spatial and temporal scales much larger than those associated with the parts. Whilst debate continues around definitions, the challenges we are facing in understanding the integrated behaviour of systems are clearer. There is too much going on to understand and measure everything and yet if we abstract too much, we will miss the essential interactions that govern what we need to know. As a consequence of this, we must somehow embrace inevitable ignorance, uncertainty, questions of appropriate scale, and making use of all available knowledge, quantitative or not. In this presentation I will talk about the common challenges we face in environmental science, and human health. I will show some approaches that might be used to meet these challenges and how, by focussing on the common challenges rather than the technologies and length scales that divide us, we might make progress.

Workshop/Network Abstracts

NE/E007899/1	Begon, M	Workshop - Predicting Zoonotic Outbreaks: Building on the Plague Threshold Model
NE/E008399/1	Givens, DI	Environmental impact on health benefits of organic food production
NE/E00864X/1	Collins, CD	Soil, health and environment network
NE/E008712/1	Horwell, CJ	A network for the study of the properties and respiratory health effects of natural mineral dust
NE/E00878X/1	Davidson, K	Relating harmful phytoplankton to shellfish toxicity and human health
NE/E008968/1	Hardy, AR	Impacts of climate change on the risks of biological and chemical environmental contaminants from agriculture to human health
NE/E009026/1	Cook, N	A UK Network for Environmental and Food Virology
NE/E009484/1	Ramsey, MH	Multiple Links Towards Integrating Teams for Understanding of Disease and Environment - Multitude

Workshop - Predicting Zoonotic Outbreaks: Building on the Plague Threshold Model
PI: Mike Begon, University of Liverpool

In the study of host-pathogen dynamics, the failure of empirical investigations to keep pace with the development of theoretical concepts has often been noted. One area where this shortfall is especially regrettable is the application of those concepts in the medical and veterinary sciences, including the development of predictive models of times and/or locations of high risk of a disease being passed from a wildlife reservoir to human (or domestic animal) populations. A rare example of at least an initial attempt to produce a model predicting zoonotic outbreaks is provided by the work of Davis *et al*. (2004), using long-term data on bubonic plague (*Yersinia pestis* infection) in Kazakhstan, and demonstrating the existence of a critical abundance threshold in the gerbils, which had to be exceeded for plague to become established in its reservoir (and be a threat).

This project comprises two workshops. Their purpose is not to dwell on the plague model as such, but rather to use it as a springboard to ask: What are the prospects of, and what data will be necessary for, utilising critical abundance thresholds, and other key concepts in epidemiology, in developing early warning models for other disease systems in wildlife that are a threat to public health? Under what circumstances would different (types of) models be necessary? How best can such models be turned into tools that are useful to public health practitioners? What do public health workers want/need? How best can predictions such as these be incorporated into a larger risk analysis and/or cost-benefit analysis? And to what extent is it necessary to go beyond knowing what is optimal on purely economic grounds in order to take 'social' factors into account?

The first workshop took place on 17-19 April 2007 in Liverpool. Thirty-two delegates from ten countries attended. Twenty papers were presented in sessions entitled: 1. Plague in Central Asia (and beyond), 2. Other systems (which included Lassa fever, Monkeypox, Lyme disease, wildlife infections in the Serengeti, Rift Valley fever and tick-borne infections), and 3. Generic issues (which included climatic effects, data quality, the use of the basic reproduction number, economic issues, socio-cultural factors, risk assessment and the use of GIS).

The aim of this meeting was that experiences would be shared, key issues identified, and people identified who would address those issues over the following twelve months, either through meta-analyses, reviews, or small pieces of exploratory original research. People would work as individuals, in pairs, or in large groups. Reporting the results of these investigations, and further discussion, would be the purpose of the second meeting, but participants also agreed that all would aim to produce tangible, written output from their work. The final half day of the first workshop was given over to the planning of this.

The second workshop will take place 9-11 April 2008, also in Liverpool. At the time of writing (4 January 2008), 29 delegates with a very similar international mix are fully confirmed, several others are expected, and 16 oral papers are confirmed, but again, several others are expected.

Effects of the Environment on the Nutritional Quality and Safety of Organically Produced Foods

A M Minihane, E Shaw and D I Givens
University of Reading

Background

Over the last two decades a marked increase in the demand for organically produced foods has been evident. Organic food is usually promoted as containing fewer contaminants, more nutrients and as being less likely to cause food poisoning as well as having a positive effect on the environment. Some of these attributes are difficult to quantify and there are also suggestions of potentially harmful consequences of organic production. Crucially it is not known with certainty how a wide range of environmental variables may influence the situation. These issues were addressed in a two day international Workshop on 18-19 December 2007 attended by some 80 delegates.

Key questions addressed

Are there quantifiable effects of organic rather than conventionally produced food on human health?

Areas covered were a) n-3 fatty acids, selenium and flavonoids and chronic disease, b) food-borne pesticides, herbicides and nitrate and c) food-borne toxins and infectious agents (e.g. mycotoxins and *E. coli* O157:H7).

How does the environment impact on these possible health benefits? Do environmental variables or differences specific to organic (as opposed to conventional agricultural practice) have a far greater affect on the health value of foods than the production method?

How do the public perceive these benefits? Regardless of whether any measurable health benefits exist from consumption of organic produce, the public perception of health gains associated with organic produce is undoubtedly influenced by statements that are not (yet) able to be supported by scientific evidence.

Outcome

The event arrived at many valuable conclusions, some key ones included:

- There are very few data which truly compare nutritional aspects of organic with conventionally produced foods. Although environment is a strong determinant of nutritional aspects there is little evidence of differences between organic and conventional practices.
- Dietary exposure to synthetic pesticides is likely to be significantly lower in organic foods although amounts in conventional foods are not known to pose a health threat
- Risk of microbiological contamination is no greater with organic than conventional foods meaning that good hygiene practices are important for both types of foods.
- Organic foods may have higher levels of flavonoids and phytoprotective substances than conventional foods but the degree is variable, since it is highly dependent on environmental factors (e.g. light, soil nutrients, chemical treatments, pathogens) and storage.
- The whole event including recommendations for future research is being written as a book to be published by CABI later this year.

Soil, Health and Environment Network (SHE-Net)

C. Collins[1], R. Duarte-Davison[2], Ian Martin[3], David Mortimer[4], T. Pless-Mulloli[5], G. Shaw[6].
1. University of Reading, 2. Health Protection Agency, 3. Environment Agency, 4. Food Standards Agency, 5. University of Nottingham, 6. Newcastle University

Overview

The aim of SHE-Net is to improve our estimates of human exposure to toxic organic chemicals in soil through the consumption of home grown and allotment produce and consequently improve the protection of public health. The largest area of concern in the risk assessment process for contaminated soils is the oral ingestion pathway, specifically the plant uptake of organic pollutants, where the knowledge is currently lacking. SHE-Net is unique in that it assembles national and international experts in the areas of plant science, toxicology and risk assessment to address these issues. SHE-Net will produce a series of authoritative recommendations to help improve predictions of the health risks from chemical contamination of soils resulting in improved public health protection. The outputs from the network will be of direct benefit to the Environment Agency, Food Standards Agency, Health Protection Agency and local authorities when providing guidance on land affected by chemical contamination.

Achievements to date

Two of the three workshops planned by SHE-Net have been held. 1) Transfer of organic pollutants from soil to plants, 27-28 September 2007 2) Human health and organic pollutants, 29-30 January 2008. The final workshop 'Risk assessment procedures for contaminated soils and the foodchain' is planned for mid May at the University of Nottingham.

The first workshop hosted 19 academics and regulators from the UK, Europe and the USA. A simple qualitative screening model was developed at the workshop to determine whether individual sites posed a risk and which plant components were likely to be contaminated. A series of recommendations were produced to guide future modelling developments for example: grouping of crops by edible portion; the expected accuracy of prediction and developing guidelines for data used in the calibration and validation of models.

The second workshop had 28 participants from a diverse range of backgrounds. It addressed the relationship between soil levels of pollutants and human body burdens and environmental exposures to human health outcomes. Three key areas to address these problems were identified. These were; toxicology, measuring bioaccessibility and communicating risks to the general public. The proceedings of the workshop have not yet been completed so final recommendations are not yet available.

Conclusions

The SHE-Net network has provided a valuable forum for bringing regulators and academics from a range of disciplines together. It has therefore answered the aims of the Environment and Health initiative in building technical capacity in this discipline. Additionally SHE-Net has already developed some tools for use by regulatory bodies.

A Network for the Study of the Properties and Respiratory Health Effects of Natural Mineral Dust

Dr C.J. Horwell, Institute of Hazard & Risk Research, Department of Earth Sciences, Durham University (P.I.) (http://www.dur.ac.uk/claire.horwell/ukndhn)
Dr P.J. Baxter, Institute of Public Health, Cambridge University.
Dr C. Oppenheimer, Geography Department, Cambridge University.

The UK Natural Dust & Health Network was established in early 2007, bringing together the multidisciplinary researchers in the UK interested in understanding how the composition and properties of natural mineral particles (NMPs) give rise to their adverse health effects. The Network also aims to widen debate on risk assessment and perception, and regulatory activity. The core goals of the Network are to:

- synthesize and report on the current understanding of the toxicology of NMPs in human and animal respiratory health
- generate hypotheses for research into the health risks of NMPs, using volcanic particles as a model
- inform public perception and regulatory activity over air quality standards and occupational exposure limits for NMPs
- enhance scientific capacity for the rapid investigation of air pollution episodes including the evaluation of atmospheric chemistry, and particle toxicity and dispersion

The network fosters collaborative exchange on a wide range of health-related aspects of natural mineral particles (NMPs). Key areas covered are:

- Exposure – source, dispersion and atmospheric chemistry of plumes containing NMPs
- Toxicity – mineralogy, size spectrum, transformations, surface reactivity and interactions of particles with gas and aqueous phases
- Policy – health risk assessment for community and occupational exposures to NMPs; public risk perception; legislative implications
- Role of scientists in planning for air pollution episodes involving NMPs

The Network addresses all NMPs whilst exploiting the insights that can be obtained from the advances in research on volcanic particles, including ultra-fines. Volcanoes provide natural laboratories for the study of natural particle generation, transport, chemical transformations, and their variable surface properties and composition.

The Network is built around a core membership representing environmental health and medicine, toxicology, mineralogy, volcanology and atmospheric science. The seven core members met for the Planning Workshop on 29 May 2007 at Cambridge University. Each participant synthesized the key studies in their areas of expertise. The group then defined the themes and format of the Plenary Workshop.

At our Plenary Workshop, to be held on 14 March 2008 at Cambridge University, the core membership will be joined by other UK and international experts (~ 30 participants) who will contribute to a wide exchange of views on topics including risk perception and environmental policy, regulatory issues and contingency planning for an air pollution event.

A further one-day wrap-up meeting of the core experts, will involve a synthesis and discussion on future research directions, policy relevance and planning of the final report.

Relating Harmful Phytoplankton to Shellfish Poisoning and Human Health

PI Keith Davidson, Scottish Association for Marine Science, Oban
Co-I Eileen Bresnan, Fisheries Research Services, Aberdeen

Some species of marine phytoplankton produce a range of toxins. These phytoplankton may be ingested by filter feeding shellfish that concentrate the toxins in their flesh without themselves being harmed. Subsequent consumption of the shellfish by humans may lead to a range of potentially fatal and non fatal heath disorders. A workshop was held at SAMS on the 14-16th of October 2007 to discuss a range of issues relating to shellfish poisoning. Forty seven delegates attended representing environmental and medical science, medical practice, monitoring organisations, government regulators and the shellfish industry. This is the first workshop to bring the main representatives of these disparate groups together in the UK. In additions four international experts attended representing the USA, New Zealand and the Republic of Ireland. The workshop highlighted the increasing importance of seafood aquaculture globally. In the UK, shellfish consumption remains relatively low but exports are significant and the industry is important to the economy or coastal regions both directly and through tourism. While the health benefits of seafood are known many UK consumers still perceive seafood as "risky" and an important role of science in this area may be to clarify the real risks/benefits of this foodstuff to the public. An important distinction between the acute and chronic effects of algal toxins was highlighted, with the latter and also the possibility of acute illness from aerosol delivery of phytoplankton toxins being particularly poorly understood. However, for all aspects of shellfish poisoning there is a general lack of medical appreciation at GP level. The lack of diagnostics tools and records of algal toxin related illnesses mean that the real extent of the problem is unknown. In the UK, a system of monitoring of shellfish toxins and potentially harmful phytoplankton is thought to be broadly successful in preventing acute illness. Recommendations of the workshop included moving away from the mouse bioassay for toxin determination, the development of rapid tests for toxins as well as molecular methods for harmful phytoplankton screening. Better systems for determining incidence and effects of toxins in humans are necessary, including follow up of toxin events. Finally, communication between stakeholders and also with the public must be improved.

Impacts of Climate Change on the Risks of Biological and Chemical Environmental Contaminants from Agriculture to Human Health
Hardy, AR

A UK Network for Environmental and Food Virology
Nigel Cook

Environmental and Food Virology is the study of viruses which can be transmitted through water, sewage, waste, soil, air, fomites or food. Such viruses include human and animal pathogens, which may contaminate food or enter the environment through faecal shedding by infected individuals or through sewage pollution, and be transmitted back to susceptible individuals to continue the cycle of disease. This cycling of viruses can result in sporadic infections or outbreaks of disease.

Within the UK, there are current issues with food and environmental transmission of viruses. In addition, new problems are likely to emerge. Cooperation and communication between various disciplines is vital to respond to the risks which viruses in food and the environment pose to public health. The Network which was established during this project combines expertise in environmental and engineering science with public health research, by being composed of water and food virologists, epidemiologists, veterinary virologists, specialists in water and sewage engineering, waste specialists, agricultural specialists, and molecular virologists. In the project year, the Network has considered issues such as current and emerging pathogens, routes of human exposure, detection methods, survival of viruses, and methods of control and elimination.

The Network met in April, at the Central Science Laboratory, York, to identify the most significant gaps in knowledge regarding transmission of viruses through the environment and food within the UK. Such gaps include:

- Are there emerging environmentally transmitted viruses in the UK?

- Can viruses be detected in UK watercourses, and to what extent?

- What is the relationship between detection of viruses by molecular methods, and health hazards?

- What is the potential in the UK for virus contamination of crops through exposure to manure?

The Network is holding a Workshop later in January, in which these and other issues will be discussed with various stakeholders (other researchers, regulators, funding bodies etc.). The feedback obtained from the Workshop will be incorporated within the project's Final Report.

The Final Report will contain a comprehensive description of current and emerging UK issues regarding pathogenic viruses transmitted via the environment and foods, followed by detailed recommendations regarding responses to these issues.

The project has strengthened the commitment to cooperative activity amongst key UK experts in the various disciplines involved. Building this capacity will help to meet the challenges posed by pathogenic viruses which can be transmitted via the environment and by food.

Multiple Links Towards Integrating Teams for Understanding of Disease and Environment (MULTITUDE)

Michael H. Ramsey, Dept. Biology & Environmental Science, University of Sussex.
Alex Stewart, Consultant in Health Protection & Communicable Disease Control, Cheshire & Merseyside Health Protection Unit

The objectives of this project are to:

- Bring together researchers from both the medical/heath and the geo/environmental specialisations, in order to
  - Provide authoritative and broadly accessible reviews of the key issues in five important research areas, from both perspectives.
  - Discuss how ideas from these different specialisations can be combined to identify and address gaps in current understanding
  - Initiate interdisciplinary collaborations that will result in fresh research strategies to address these important topic areas, ready for preparation of new E&HH proposals
- Publish proceedings of the workshop, which can act as a focussed review and starting point for further development of research, using this integrated approach

The project organised a Workshop that brought together 50 participants with expertise on Environment and Human Health from a wide range of different disciplines. The workshop was held in conjunction with the Society for Environmental Geochemistry and Health[1]. It began with a fieldtrip to a local case study site (ICI / Weston quarry / village) with presentations explaining the views of industry, health and the community. This exemplified the current issues that are being tackled, the approaches and methods being applied, and the need for new interdisciplinary research to improve the way such situations are investigated, and the human health outcomes improved. Five workshop sessions then concentrated discussion on key topics for research:-

1. *Transport and dynamics of toxic pollutants in the natural environment and their effect on human health* (Andrew Hursthouse/George Kowalczyk).
2. *Uncertainty in risk assessment, epidemiology and regulation* (Mike Ramsey/David Briggs).
3. *Social, economic and behavioural factors in the genesis and health impact of environmental hazards* (Meg Huby/Rupert Adams).
4. *Strategies for improving health in contaminated situations* (John Farmer/Richard Jarvis).
5. *The effects of multiple toxic pollutants on health* (Alex Stewart/Sohel Saikat/Joy Carter/ George Kowalczyk).

The session leaders, one a health/medicine expert and the other a geo-environmental scientist, initiated a substantial discussion with the participants to synthesise the two approaches and to identify new collaborative research that could better investigate the situation, and provide optimal ways to improve human health outcomes. The findings from each session were brought together and synthesised into overall conclusions for the whole workshop[2]. Papers are being written that summaries the findings and conclusions from each workshop, for publication in a special issue of the Journal of Environmental Geochemistry and Health. A follow-up Workshop in Athens on 2/3 April 2008, will further develop the teams brought together in Liverpool, and focus in particular on perception and communication in the assessment of environment and human health risks. It will include input from existing EU-funded teams on related topics, including INTERESE, NoMiracle, NORMAN and HEIMTSA.

[1] http://seghconference.co.uk/information.html
[2] http://www.segh.net/newsletter.php

Working Group Abstracts

NE/E008526/1	Clough, HE	BAMRA: Bayesian Approaches in Microbial Risk Assessment (Working Group)
NE/E00881X/1	Lai, KM	Outdoor airborne pathogens and human health in the UK
NE/E008992/1	Banwart, S	Going Underground: Human Pathogens in the Soil-Water Environment
NE/E009131/1	Macdonald, DW	Quantifying Biophilia
NE/E009352/1	Leake, J	Grow your own - health risks and benefits of producing and consuming your own food in urban areas

BAMRA: Bayesian Approaches in Microbial Risk Assessment

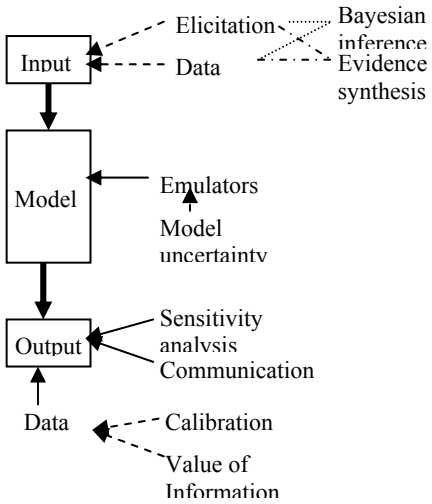
Clough, H. E.., Kennedy, M. C., Anderson, C. W., Barker, G., Cook, P. , Hart, A., Hart, C. A., Malakar, P., Oakley, J. E., Pielaat, A., O'Hagan, A., Snary, E. L. and Turner, J.

The BAMRA group unites experts in risk assessment, Bayesian statistics, public health and food safety to discuss Bayesian statistics and Microbial Risk Assessment (MRA).

MRA is a model-based tool for managing food chain risks. MRA models commonly describe complex farm-to-fork food production chains, are multi-factorial, and involve uncertain parameters and processes. Interest concerns the impact of uncertainty in model inputs and structure on uncertainty in model outputs (estimates of "risk"). Bayesian statistics provides a unified approach to uncertainty: by contrast with classical approaches it describes uncertainty probabilistically, permits strengthening of inference via incorporation of prior belief, and synthesizes multiple types of uncertainty in a mathematical framework. Various papers have used Bayesian approaches in MRA but have principally focused on parameter uncertainty.

BAMRA is exploring the potential offered by various Bayesian approaches, including Bayesian Belief Networks, and the recently developed BACCO ("Bayesian Analysis of Computer Code Outputs") [1-3] approaches. Potential applications are summarized in Fig. 1. Given a model, the methods dramatically reduce the number of code runs/CPU time required to quantify different types of uncertainty, BACCO approaches in particular typically requiring 1-2 orders of magnitude fewer code runs than Monte Carlo methods for equal precision. They hence permit important analyses of complex models which are not feasible with MC methods. We describe two typical BAMRA case studies (others are in progress) motivated by a model assessing the risks from Vero-cytotoxigenic *E.coli* (VTEC) O157 in pasteurised milk.

Figure 1



Transmission of VTEC O157 in a dairy herd is described by a mathematical model [4] estimating prevalence of VTEC O157 in unweaned, weaned, dry and lactating groups. This model is useful for mimicking a "typical" dairy farm in an MRA model. Weaned animals are important in maintaining herd infection, hence weaned group prevalence may correlate with final milk contamination. We use BACCO Sensitivity Analysis to study the link between uncertainty in the 48 model inputs and outputs.

BACCO shows that most (54%) of the uncertainty in weaned group prevalence is explained by the average weaned group infectious period. Other inputs are similarly ranked by their contribution.

An analogous study of a model for the entire milk production model is ongoing. It is likely that an important driver in whether VTEC O157 ultimately poses a risk in milk is pasteurisation. Successful pasteurisation kills pathogenic bacteria, but pasteurisation failure (PF) or post-pasteurisation contamination (PPC) can occur. Current data indicate only a pasteurisation breach and do not separate PF and PPC, but the relative frequency of each is important for control strategies. BAMRA will, with pasteurisation experts, conduct elicitation to determine, given a breach, the probability that PPC (or PF) is indicated. Elicited distributions will be fed into the milk model to determine the contribution of PF and PPC to total uncertainty, hence informing research priorities.

Outputs from BAMRA so far include **SHELF** (The Sheffield Elicitation Framework http://www.tonyohagan.co.uk/shelf/index.html), a **prototype workshop** on Bayesian methods for Risk Assessors, and a **draft review** paper. Subject to final funders' approval, this project has already inspired an **extension collaboration with the RELU-RISK project**.

[1] Kennedy and O'Hagan (2001); [2] Oakley and O'Hagan (2004); [3] O'Hagan (2006); [4] Turner *et al*. (2003).

Outdoor Airborne Pathogens and Human Health in the UK (*Airpath*)
PI: Dr. Ka-man Lai (University College London)
Co-I: Prof. Jean Emberlin (University of Worcester) & Prof. Ian Colbeck (University of Essex)

What is it about?
This is a network programme which focuses on airborne pathogens, the outdoor environment and human health. The natural environment plays a significant role in controlling and determining the source, pathway, exposure routes and, ultimately, health risk of airborne pathogens to humans. It is very important to understand the environmental pathways and properties of these pathogens and their link and mechanism in causing diseases in order to protect human health. This working group aims to build a network and research capacity to tackle human health problems associated with airborne pathogens and the outdoor environment.

What have we done so far?
Meetings
Two meetings were held at UCL in July and October 2007. A total of 16 members and 3 A-level students have attended the meetings. The members are from the UK and US universities, a UK company, Ministry of Defence (MoD), Health Protection Agency (HPA) and hospitals. The network has representatives from physics, microbiology, medicine, epidemiology, aerobiology and meteorology. The presentations and discussions were organised around 6 thematic areas plus a category for "others":
1. What is in the air and outdoor airborne pathogens: state of knowledge
2. Current, developing and future techniques
3. Risk factors: humans, environments and activities
4. Prepare for the new challenge: environmental change and new and emerging diseases
5. Control and prevention in outdoor environments
6. Policy and international issues and research

Each member gave a presentation on one of the topics above and this was followed by discussion.
Website: We have developed a website http://www.ucl.ac.uk/cege/Research/environmental_structural_geotechnical/environmental_engineering/airpath/ to facilitate the network activities. The meeting programmes, presentations and reports are posted on this website.

What are the outcomes?
Network: We have successfully developed a multidisciplinary network which links different disciplines together and provides a platform to facilitate discussion and collaboration.
Report and proposals: A report is being prepared to summarise the outcomes of the meetings. This report will be submitted for publication in an international journal. There are various proposals developed and being developed directly due to this network.
Student engagement: In the first meeting, we invited 3 A-level students, supported by the Nuffield Foundation to participate into the meeting. Subsequently these students undertook a project on airborne faecal coliform bacteria survey at UCL.

Future plans include:
- a session on outdoor airborne pathogens in the next HPA meeting in September 2008
- continue the network and proposal development by facilitating meetings and research capacity building

Going Underground – Human Health Risks from Pathogens in the Soil-Water Environment

PI: Prof. Steven Banwart, University of Sheffield.
Project term: April 2007 – July 2008

Microbial movement through catchments is intimately connected with soils and sediment migration. The soil-water environment (soils, water in soils, freshwater sediments and other unconsolidated materials) may act variously as a filter, a sink, a source, a vector, a store or a receptor for pathogenic organisms. Bodies of water connected to these soil-water environments include farm drains, ditches, streams, springs, shallow groundwater, the hyporheic zone, lakes, reservoirs, canals, rivers, estuaries, urban storm drains, sewers, waste outfall pipes, water abstraction systems, etc. Human health risks arise as a combination of exposure to infection; infection rate; severity of resulting disease; and perception of the hazard.

The physical and biological sciences emphasise the occurrence, movement and persistence of pathogenic microbes in the environment. Catchment science and risk assessment attempt to quantify these processes in terms of functional parameters which form a basis for mitigation, management or removal of the pathogen hazard. Medical statistics and public health are concerned with actual incidences of disease and the development of socio-economic responses to reduce rates of exposure and illness. The Going Underground project aims to identify and develop research priorities which bridge the gaps between these disciplines. The Working Group comprises a core group of researchers from Sheffield, Lancaster, Oxford, Liverpool, IGER, Aberystwyth, EA Starcross, and DEFRA.

The 1st residential workshop, held from 21st-22nd November 2007, was focused on conceptualising and highlighting areas of weakness in our current understanding of pathogen occurrence in soil-water environments and consequent risks to human health. The core Working Group was complemented by several invited experts: Andy Vinten (Macaulay Institute), Alan Godfree (United Utilities), Jim Wharfe (Environment Agency), Gordon Nichols (Health Protection Agency), Chris Sherlock (Lancaster) and Clive Edwards (Liverpool). The workshop resulted in the identification of 15 priority research areas which included:

- the further development of quantitative epidemiology coupled to policy measures based on critical control points;
- urgent work to assess the role of extreme events (e.g. flooding) in the transport and persistence of pathogens in environments closely proximal to human receptors;
- improved assessment of the impact of land management policies on pathogen loads in the soil-water environment and the development of a budget/barrier model to quantify pathogen transfer along pathways through the soil-water environment.

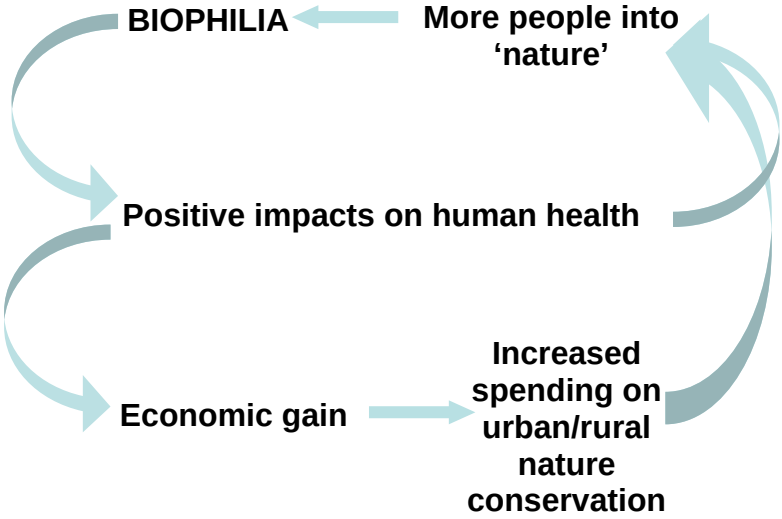
Subsequent residential workshops will address issues of climate and land-use change in determining future human health risks from pathogens occupying new environment niches (January 2008), and issues of understanding patterns of human exposure and infection as related to spatial distributions of pathogen loads and contact points (May 2008).

Quantifying Biophilia
Principal Investigator: Professor DW Macdonald, WildCRU, University of Oxford
Postdoctoral Researcher: Dr. Joelene Hughes, WildCRU, University of Oxford

The notion that spending time with 'nature' can reduce stress may seem self evident. Natural recuperative tonics have been prescribed throughout recorded history from Grecian healing groves to Victorian seaside resorts. Today, mental health disorders related to stress, such as depression, are increasing rapidly. Could experiencing nature prevent this? Like so many intuitive "truths" however this assertion masks a complicated set of unanswered questions. The "Quantifying Biophilia" scoping study was tasked with the aim of "…finding the right questions to ask and the right order to ask them in." (Dennet 2006).

The **first meeting** brought together **16 cutting edge experts** from a range of disciplines and professions to synthesise the available evidence, and frame a series of multi-disciplinary research goals.

Attendees were provided with **an initial perspective – the virtuous circle –** on how the link between biophilia and applied nature conservation could work. Then a variety of scintillating talks and discussions expanded on this scaffold.



Benefits of Biophilia - the virtuous circle

Discussion divulged there is currently a **paucity of evidence** linking the evolutionary basis for biophilia, experience of nature and a positive benefit for human health. However we now have **novel and innovative tools** at our disposal for examining physiological stress responses, **alongside a growing knowledge** of how the complex mammalian brain may work and respond at a cellular level. These developments enable us to start hypothesising on the mechanisms by which interaction with nature may affect our mental health.

Economic gains are not explicit - alert to the laws of unintended consequences consideration must be made of perverse outcomes such as increasing transport. **Increasing urbanisation** may have led to greater disconnection from nature however the **potential to get people back into nature is there**: walking is nationally one of the most favoured activities; people who take part in 'Health Walks' continue to do so because they appreciate time in the countryside. Corporations are also becoming aware of the importance of the environment for their staff health and well-being, proactively redesigning the working environment and providing opportunities. The future of this project sees further synthesis of these areas with some scoping experimental research. The project is due for completion by August 2008.

Grow Your Own: Health Risks and Benefits of Producing and Consuming Your Own Food in Urban Areas

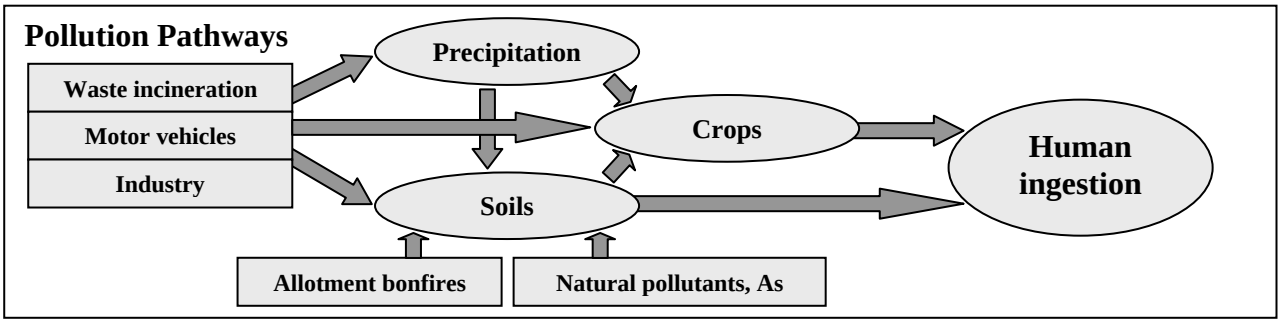
Principal Investigator: Dr Jonathan Leake, University of Sheffield
Project coordinator: Dr Andrew Adam-Bradford, University of Sheffield
Website: http://www.shef.ac.uk/environmentdivision/gyo Email: andy@adambradford.eu

Project Aim:
This working group aims to conduct an in-depth analysis and synthesis of the health risks and benefits of producing and consuming your own food in urban areas.

Project Focus:
The particular focus of the project is on urban soil pollutants - including both toxic elements and persistent organic pollutants that can pass up through the food chain or be ingested in soil. We are considering pathways of pollutant transport and deposition and human uptake from urban cultivation. Against the health risks associated with exposure to environmental pollutants and toxic agents in urban environments needs to be balanced the increasing evidence of therapeutic health benefits of producing and consuming fruit and vegetables. This working group is, for the first time, bringing together environmental scientists and health professionals to provide a balanced assessment of risks and benefits of urban food cultivation. The proposal is particularly relevant to E&HH themes: chronic low level exposures to toxins; soil degradation and trace metal deficiencies; assessment of exposure and bioavailability from physical and behavioural pathways.

Project Objectives:
(1) Conduct a critical review of evidence-based existing research.
(2) Develop a coherent interdisciplinary research agenda to improve our understanding of the main issues.
(3) Build capacity to conduct more effective research on effects of urban food production on human health.

Project Progress:
(1) Group meetings underway: first held May 2007, second held December 2007 and included two presentations: Organic allotment production in Sheffield City, Richard Clare, Sheffield Organic Food Initiative & International perspectives on urban agriculture, Andrew Adam-Bradford, GYO
(2) First draft of critical review scheduled for mid February 2008
(3) Poster being prepared for submission to the British Ecological Society Annual Symposium: Ecology of Industrial Pollution, Birmingham, 7-8 April 2008



Discipline Hopping Abstracts

NE/E008054/1	Hawkey, PM	The application of clinical microbiological methods to the study of MRSA in the environment (discipline hop)
NE/E007732/1	Thomas, GO	Linking environmental fate and behaviour studies with the toxicology and epidemiology of organic pollutants

The Application of Clinical Microbiological Methods to the Study of MRSA in the Environment

Hawkey, PM

Linking Environmental Fate and Behaviour Studies with the Toxicology and Epidemiology of Organic Pollutants

PI Gareth Thomas, Lancaster University

Gareth Thomas is spending 6 months working at the Institute of Risk Assessment Sciences (Utrecht, The Netherlands), studying a broad range of theoretical and practical aspects of toxicology and epidemiology. The objectives are for him to establish strong collaborative links, and to develop his understanding of toxic effects to enhance the potential for future collaborations in his research into the behaviour and effects of chemical pollutants in humans and other biota. To get an appreciation of the practical aspects of toxicology, he is performing a research project on the neurotoxic effects of organophosphorus and organochlorine pesticides - current use and legacy pesticides, respectively, to which the general population is exposed primarily through the diet. After characterising the dose-response relationships for the non-acetylcholinesterase neurotoxicity of chlorpyrifos and lindane, the mechanisms of the effects seen, and the potential for interactive (i.e. additive, synergistic or antagonistic) effects are now being investigated.

Exploratory Award Abstracts

NE/E007791/1	Donaldson, K	A proof of concept study for a structure activity model for the toxicity of nanoparticles
NE/E008038/1	Begon, M	Ljungan Virus - an undetected but dangerous zoonotic agent
NE/E008232/1	Stone, V	Assessing human exposure, uptake and toxicity of nanoparticles from contaminated environments
NE/E008313/1	Atkinson, JM	Micronutrient deficiency in maternity and child health: scope for agricultural and educational intervention in soil-food-human transfer
NE/E00833X/1	Matthews, I	An exploratory study investigating the physiochemical characteristics of ambient air particles responsible for the dysregulation of pulmonary genes
NE/E008534/1	Tyrrel, S	Endotoxin emissions from commercial composting activities
NE/E008593/1	Doherty, R	Impacts of Future Environmental Change on Climate- and Air Pollution-Mediated Human Health
NE/E008682/1	Grant, A	Human health risks from contaminated tap water. Can we use microbial ecology to assess the integrity of water distribution systems?
NE/E008720/1	Mitchell, RJL	Exploratory award: Multiple environmental classification of areas for researching spatial health inequalities
NE/E008739/1	Harrison, R	Determinants of Oxidative Potential, A Health-Based Metric to Assess Particulate Matter Toxicity
NE/E008844/1	Nieuwenhuijsen,MJ	Born in Bradford: environmental exposure and birth weight
NE/E008917/1	Pearson, DG	A preliminary assessment of levels of bioavailable anthropogenic platinum-group, lanthanide and high field strength metals in human tissue and DNA.
NE/E008933/1	Wang, H	Plant virus infection as a determinant of pollen allergenicity
NE/E00895X/1	Spurgeon, DJ	Modelling and measurement of Cd exposure and pathology in human volunteers living in proximity to a smelter source
NE/E009042/1	Few, R	Seasonal environmental hazards: a multi-disciplinary approach to the analysis of health risks in lower-income countries
NE/E009085/1	Salisbury, VC	A study of helminths as novel vectors and reservoirs of human pathogens in the environment, using in-vivo real-time imaging systems
NE/E009166/1	Valsami-Jones, E	Hazards of nanoparticles to the environment and human health
NE/E009271/1	Gibson, GR	Model human digestive system for the determination of bioaccessibility of environmental pollutants.
NE/E009328/1	Tyler, AN	Strategies to manage toxic cyanobacetrial blooms in lakes: remote sensing, modelling and cost benefit analysis
NE/E009336/1	Stephens, WE	Exploring the link between surface structures and toxicity in mineral particles: Case study of induced and intrinsic toxicity in quartz
NE/E009395/1	Kendall, K	Nanotoxicology of Fine PM: The Role of Surfactant and Collectins in Short-Term Health Effects of PM Air Pollution
NE/E009565/1	Gallagher, MWG	Identification and Verification of Ultrafine Particle Affinity Zones in Urban Neighbourhoods / A Proof of Concept Proposal

A Proof of Concept Study for a Structure Activity Model for the Toxicity of Nanoparticles

Professor Kenneth Donaldson[1], Prof Xue Z Wang[2], and Professor Ian Megson[3]
[1]College of Med and Veterinary Med, University of Edinburgh, [2]Institute of Particle Science and Engineering, University of Leeds, [3]UHI Millennium Institute, University of the Highlands Islands

Background There is a large number of nanoparticles and their variants, different sizes and coatings for instance, that require testing and ethical pressure towards non-animal testing means that expensive animal bioassay is precluded [1]. One way forward is to relate the physicochemical characteristics of NP with their toxicity in a Quantitative Structure Activity Relationship (QSAR) model. A pilot study to determine the robustness of the general principle is warranted and was funded in the EHH programme.

Table 1 Nanoparticle used in the project

Class	Particle
Carbonaceous	Carbon black
	Diesel exhaust particles
	Nanotubes
	Fullerene
Polystyrene	Polystrene latex Unmodified Aminated Carboxylated
Metal oxide	Aluminium oxide (alumina) 7nm 50nm 300nm
	Cerium oxide
	Nickel oxide
	Silicon oxide (silica)
	Zinc oxide
	Titanium dioxide Rutile Anatase
Metal	Silver

Materials and Methods The panel of nanoparticles to be tested are shown in Table 1 and the structures/particle characteristics that will be assessed are shown in Table 2.These structural attributes will be related to a range of simple in vitro tests of toxicity that are shown in Table 3. The full physicochemical characteristics of the nanoparticle panel will lead to a large number of descriptors, which can be in different data format. The data will be analysed using multivariate data analysis techniques such as principal and independent component analysis, and inductive data mining (IDM). The Leeds group has developed a novel method for *in silico* QSAR modelling of the toxicity of chemicals[2].

Table 2 Structures to be assessed

Structure	Method
Size distribution	Electron microscopy
Surface area	BET
Shape /dimensions	Electron microscopy
Surface chemistry	X-ray photon/Raman spectroscopy
Bulk chemical compositoin	ICPMS
Agglomeration status	Electro-accoustic spectrometry
Electrical charge	Light scattering
Biopersistence	Dissoluton rate
Redox potential	Electrodes
Oxidative stress potential	EPR / chemical sensors

Table 3 Activities /toxicology endpoints to be assessed

Endpoint	Assay method
Necrosis apoptosis	Live dead fluorescent assay
Intracellular oxidative stress	DCFH/GSH
Mitochondrial membrane potential	JC-1 dye
Antioxidant gene expression	RT-PCE, Western blotting
IL-8	RT-PCR
NF-kB nuclear translocation	ELISA

References

1. Royal Society and Royal Academy of Engineering: Nanoscience and nanotechnologies: opportunities and uncertainties. The Royal Society 2004.
2. Wang XZ, Buontempo FV, Young A, Osborn D: Induction of decision trees using genetic programming for modelling eco-toxicity data: adaptive discretization of real-valued endpoints SAR QSAR Env Res 2006.

Ljungan Virus - An Undetected but Dangerous Zoonotic Agent
PI: Mike Begon, University of Liverpool

Niklasson *et al*. (1998) reported that the incidence of human myocarditis, diabetes and Guillain-Barre syndrome in Sweden varied with the 3-4 year abundance cycles of the bank vole (*Clethrionomys glareolus*). Subsequently, a novel picornavirus, Ljungan virus (LV), was isolated from Swedish diabetic bank voles, and viral antigen and picorna viral-like particles were detected in the destroyed pancreatic beta cells. LV has also recently been isolated, and myocarditis and clinical diabetes reported, in several other species of wild voles and lemmings in northern Sweden, symptoms being especially associated with stress. Most recently, data from type 1 diabetes human patients and age-matched controls have been obtained in Sweden. The data demonstrate a highly significant association between type 1 diabetes and the presence of LV. Also, variations in the incidence of intrauterine fetal deaths (IUFD) in Sweden closely track rodent population fluctuations, and LV has been detected in the brain tissue in 4 out of 10 cases of IUFD and in the placenta in 5 of the 10 IUFD cases but in none of 20 placentas from normal pregnancies.

Generally, the aetiology of type 1 diabetes in children and young adults is not well understood, although both genetic and environmental factors are likely to be involved. A number of viruses have been specifically associated with disease onset. Space-time clustering, especially suggestive of an infectious component to aetiology, has been identified in childhood diabetes and in adolescents/young adults (McNally *et al.* 2006).

From our own studies in Kielder Forest, we have long-term historical records of rodent abundance and the opportunity to carry out a more detailed study of the dynamics of LV in its natural reservoir than anything attempted hitherto. The aim of this pilot project therefore is: (a) to survey our own study populations and those of other rodent species nearby (including peri-domestic rats and mice) in order to initiate a mapping of LV (and putative human risk) in UK rodents; and (b) to analyse human epidemiological data bases on type 1 diabetes in the region of our study populations to seek correlations either spatially or temporally between incidence and measures of rodent abundance or activity.

If the pilot studies provide negative results in either or especially both respects, then it will be unlikely that patterns observed in Sweden also apply in the UK, and research on this topic can be considered of low priority. But if either or especially both studies provide positive results, then Ljungan virus has the potential to become the most important wildlife zoonosis in the UK and further work will be essential.

The project started on 1 July 2007. The epidemiological database has been constructed (Newcastle) and analysis of it has now started.

A first group of rodents were trapped in September 2007: field voles, bank voles, wood mice and house mice, both from our field sites and from farms. Brains, blood and pancreas have been taken from all of them. PCRs have been optimised (or near-optimised). The brain samples have been analysed. Though not all positives have thus far been confirmed by sequence analysis, 9 of 37 bank voles, 24 of 79 field voles, 19 of 66 wood mice and 11 of 26 house mice have been positive for LV, including animals from both habitat types. Further, more focused samples will be collected in the spring.

Assessing Human Exposure, Uptake and Toxicity of Nanoparticles from Contaminated Environments

Birgit Gaiser[1], Philipp Rosenkranz[1], Jamie Lead[2], Charles Tyler[3], Mark Jepson[4], Teresa Fernandes[1], Vicki Stone[1]

[1] Napier University, School of Life Sciences; [2] University of Birmingham, Environmental Life Sciences; [3] University of Exeter, School of Biosciences; [4] Bristol University, Department of Biochemistry

With production and use of nanoparticles (NP) increasing rapidly, environmental concentrations of manufactured NP can be expected to rise. This project links existing research in nano- and ecotoxicology with the aim to assess potential risks posed to the environment, and humans, by NP in the water. Silver and cerium dioxide NP and bulk controls (Ag: 35 nm and 0.6-1.6 µm diameter; CeO_2: <25 nm and <5 µm diameter) were chosen as model particles. Endpoints assessed so far include acute toxicity of the particles to the aquatic invertebrate *Daphnia magna* and cytotoxicity of the particles to the human hepatocyte cell line C3A.

Dose- and size-dependent toxicity of Ag NP in *D. magna* and hepatocytes.

No cytotoxic effects were observed for CeO_2. The particles also did not cause death of *D. magna* neonates in a 96 h acute study. Ag particles showed both dose- and size-dependent toxicity, with an LD_{50} in C3A cells of 50 ug/ml (35 nm) and 330 ug/ml (0.6-1.6 µm). In *D. magna*, 0.1 mg/l of nano-Ag caused death of approx. 60% of neonates, whereas the same dose of micro-sized Ag caused only 15% mortality.

Particle exposure can inhibit growth and molting of *D. magna* neonates.

The acute *D. magna* exposure study revealed a potential for nano-sized CeO_2 to reduce the moulting frequency at 10 mg/l (cumulative moulting of 136.0%±48.5 compared to 202.2%±45.4 obtained for the control). Growth inhibition by CeO_2 occurred at 0.01 and 10 mg/l of NP (neonates measured 1.338 and 1.148 mm respectively, compared to 1.608 mm for the control), and 0.01 mg/l of the bulk material (1.315 mm). In a pilot study, Ag particles significantly inhibited growth at 0.1 mg/l of NP (1.135 mm) and 1 mg/l of bulk material (1.293 mm; control: 1.597 mm).

Further studies will include long-term *in vivo* exposures of *D. magna* and carp, *Cyprinus carpio*, exposures of primary fish hepatocytes, a gastro-intestinal translocation study and thorough characterisation of the particles in the respective media to assess bioaccumulation and potential human exposure to particles through the food chain.

Micronutrient Deficiency in Maternity and Child Health: Scope for Agricultural and Educational Intervention in Soil-Food-Human Transfer

PI: John Atkinson[1]; Co-I: Avril Taylor[1], Andrew Hursthouse[1] and Chris Robertson[2]
1. University of the West of Scotland (Paisley); 2. University of Strathclyde.

"No Society has ever seen a broad-based reduction in poverty without major and sustained investments in the rights of people to health, nutrition and basic education" UNICEF

Global food insecurity is associated with micronutrient deficiencies and it has been suggested that 4.5 billion people world wide are affected by deficiencies in iron, vitamin A and iodine. Zinc has also been identified to be of increasing concern. The most vulnerable are young children and women of childbearing age. This project, through multi and interdisciplinary research is seeking to establish the opportunity for concerted action to deliver step change improvements in the nutrition of developing countries. A research team crossing environmental, nutritional, medical and social science has been assembled to study the relationship between soil quality, food production and the nutritional health, behavioural and cultural attitudes of women and children in Malawi.

We have identified two geographically separate regions close to Blantyre in S.Malawi and started to engage with a number of village communities through support from local NGOs. To date, our data collection has included field campaigns to collect spatial information relating mothers to their main food supply, provide observations on farming methods and dietary diversity. Our programme of soil and plant material collection is underway and first stage samples are currently being characterised for nutrient content and other parameters.

The next stage includes the development of health and lifestyle questionnaires, blood sampling protocols through intensive consultation with Malawi-based charitable and educational organisations, including modification for cultural and local sensitivities. In parallel, we are collecting social and anthropological observational information, compiled though diary reports.

Our overall assessment will require the development of protocols for spatial assessment and the statistical interpretation of chemical data from environmental, food and nutritional compartments, combining medical observations and the social context.

In the early stages of the project we have been able to assemble a research team which includes contributions from EU based soil scientists, environmental geochemists, midwives; medical, social and anthropological sciences as well as epidemiological and spatial analysis specialists. Engaging on the ground with such a diverse group has highlighted numerous logistical issues in this multifaceted research, typified by the equally diverse protocols and permissions which vary across disciplines. It is clear that local engagement and cultural/social aspects dominate health and nutritional interventions and it is essential we work from the ground up.

An Exploratory Study Investigating the Physicochemical Characterization of Ambient Air Particles Responsible For the Dysregulation of Pulmonary Genes.

I. Matthews, K. Berube, T. Jones, B. Hoogendoorn, C. Gregory & R. Arthur, Cardiff University.

Ambient respirable particulates in urban areas present a cardio-respiratory risk. The biological mechanisms and causal pathways involved are largely unknown. To date studies have not made use of the holistic approach offered by genetic and proteomic technologies. Neither have they been able to collect suitably size fractionated environmental particulates for use in biological experiments.

The study commenced in August 2007 when a DEKATI ELPI was installed to sample outdoor air in a heavily trafficked residential street canyon in Swansea. The system has 12 impaction stages collecting particles in ranges of size from 7nm to 10µm. Fig 1 shows the NPs ($D_{50\%}$, 7nm) collected on the Al foil stage 1, and Fig 2 shows the TPN measured for each of 6 stages in the range of $D_{50\%}$ 7 nm – 260 nm over the period of a week. The DEKATI was checked and calibrated against (TSI Mobility Particle Sizers) at the Institute für Energie – und Umwelttechnik, Duisberg, Germany in November 2007. Some morphological analysis of NPs has been undertaken using SEM and AFM. Problems associated with removal of the NPs from the foil and solubilising them in PBS for challenging biological cells have been solved.

3-dimensional, *in-vitro*, tissue culture of normal human ciliated respiratory epithelium has been successfully grown and maintained as shown in Fig 3. Collected NPs have been used to challenge these explants and conventional toxicological responses measured to establish an appropriate challenge dose for genetic and proteomic research.

Future work will involve measuring production and release of endogenous cytokines into the basal medium of the cultures using a human cytokine array (ProteoPlex, Merck). We will also investigate gene responses using small-scale microarrays (Superarray: Oligo GEArray® Human Toxicology: Biosciences Corp, US) and changes in protein expression using PerkinElmer ExacTag Isobaric Mass Tags which enable simultaneous quantification of proteins using isobaric mass tags with a tandem mass spectrometer.

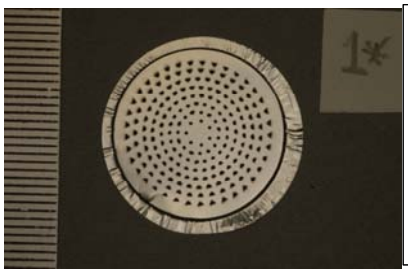


Figure 1: NP's on foil stage

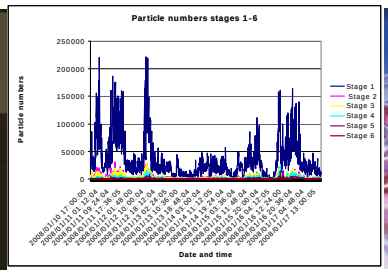


Figure 2: TPN for 1 week

Figure 3: Tissue Culture

Endotoxin Emissions from Commercial Composting Activities

Deacon, LJ., Drew, G., Hayes, E., Jackson, S., Liu, J., Pankhurst L. and Tyrrel, S.

There is a growing recognition that there are potential health risks associated with inhalation of bioaerosols. These health risks include infections and irritations of the respiratory system. There is evidence that bioaerosols are generated at some waste facilities and therefore research is required to find the best way of managing these facilities to minimise health risks to people who work there and also people living nearby. This project aims to develop new knowledge of a specific bioaerosol component of concern known as endotoxin. Endotoxin is a chemical produced by certain bacteria. It is well known that endotoxins can cause lung damage if inhaled. What is not known is the extent of the risk to the public from endotoxin released from composting facilities. This project aims to find out how much endotoxin is released from composting facilities, how far it will travel and whether the concentrations found in air from compost facilities could be expected to harm the health of people living close to these facilities.

This will be accomplished by:

(i) Examining the emissions of endotoxins from static windrow compost piles and from compost processing activities using the PyroGene assay system.

(ii) Comparing the measured emissions of endotoxins to emissions of fungi (*Aspergillus fumigatus*) and bacteria (actinomycetes and Gram –ve) sampled simultaneously with the endotoxins

(iii) Relating the particle size of bioaerosols emitted from the composting facility to their endotoxin content

(iv) Predicting the concentrations of fungi, bacteria and endotoxins around the facility using a dispersion model

(v) Relating the concentration of endotoxin measured in air around composting facilities to possible human health impacts in an *in vitro* model

Three forms of sampling, repeated in triplicate are in progress currently. They are designed to sample for both viable microorganisms and endotoxin simultaneously.

(i) Baseline – Samples taking during processing activities such as shredding, turning and screening as well as upwind 100m, downwind 50m, 100m, 150m and an ambient level between the windrows themselves.

(ii) Transect -Samples taken every 100m across the site (both upwind and downwind) from a central point – out to 400m.

(iii) Static hood – Samples from static windrows taken to allow the direct measurement of bioaerosol flux on both windward and leeward sides of windrows of different maturity.

Current results indicate that generation of bioaerosols from composting facilities is greatly increased in the direct vicinity of site activity (particularly for *Aspergillus fumigatus*) and the meteorological conditions contribute to the bioaerosol dispersal downwind. Our preliminary experiments also show that endotoxin emissions are dependent on the compost processing activity, windrow age and site location. All meteorological data is recorded to inform multiple regression analysis at the end of the project to relate environmental gradients to bioaerosol generation.

Impacts of Future Environmental Change on Climate- and Air Pollution-Mediated Human Health
(December 2007 - February 2009)

R. Doherty, M. Heal, D. Stevenson and M. Vieno, University of Edinburgh
P. Wilkinson, B.Armstrong, S. Kovats, A.Isigami, Z. Chalabi and S. Pattenden, London School of hygene and Tropical Medicine.

Air pollution is the environmental factor with the greatest impact on health in Europe. Tropospheric ozone is a major contributor to this health burden. Because ozone is generated by photochemical processes, its levels can rise substantially on hot sunny days, potentially exacerbating the direct health impacts of high temperatures. Future changes in climate and trace gas emissions will modify both ozone levels and the frequency and intensity of extreme weather events such as heat waves. *The aim of this exploratory study is to quantify the interaction between ozone-heat and mortality and produce high-resolution projections of future climate and ozone concentrations over the UK.*

Our research examines key elements shown in Fig.1

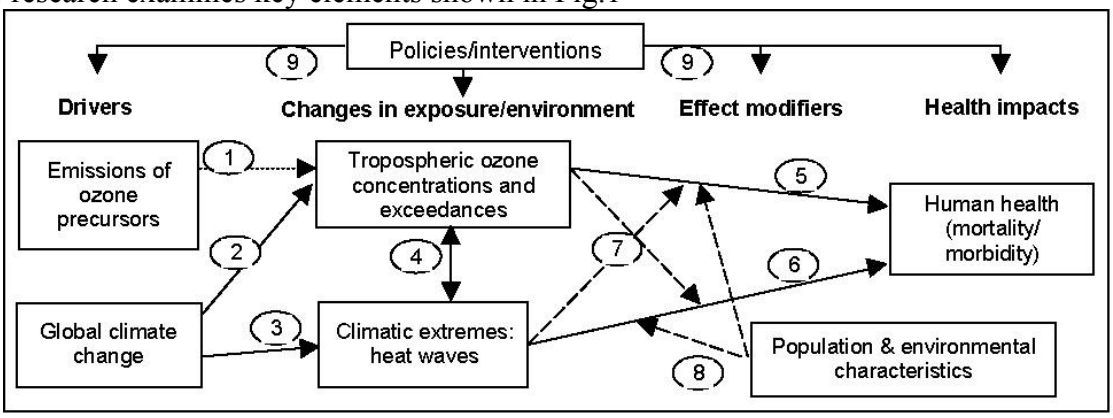


Figure 1. Simplified scheme of the main connections between environmental change, population exposures to high ambient temperatures/ozone, and health impacts. Effect modifiers are indicated by dashed lines.

We have collated daily mortality records, reports of respiratory infections together with daily weather station, ozone and PM_{10} air pollution measurements for 15 conurbations across England and Wales for 1993-2006. Using these data we will explore impacts on mortality of ozone and high temperatures controlling for confounding using a time–series regression model. In addition we have performed high-resolution chemistry transport model runs for 2003 in order to explore the potential for analysing ozone and heat effects at a 5 km by 5 km resolution across the UK. We use the EMEP4UK model driven by meteorological reanalyses and initial and boundary chemical conditions from the widely-used EMEP model. Simulated daily mean and maximum temperatures and maximum daily 8-hour mean ozone concentrations compare favourably with UK weather station and air pollution monitoring site measurements. Further model simulations under future emission and climate forcing scenarios will enable us to quantify changes in future mortality burdens from ozone and high temperatures.

New Microbial Markers of Drinking Water Contamination

E Chi Fru[1], P Hunter[2] and A Grant[1]

University of East Anglia, School of Environmental Sciences[1], School of Medicine, Health Policy and Practice[2] , NR4 7TJ Norwich UK

INTRODUCTION: Drinking water borne gastrointestinal (GI) infections remain a significant public health issue even in the UK. It is estimated that up to 40% of GI infection could be attributed to the consumption of contaminated tap water. Growing evidence indicates that a significant portion of these illnesses result from the intrusion of pathogens into DW via defective distribution networks. Pathogen monitoring in DW sometimes fails when they occur in concentrations below the detection limit of the currently used protocols. In addition, many pathogens might occur intermittently and constitute a heterogeneous mix of different organisms difficult to detect with only one technique; creating an urgency to develop rapid and reliable methods for the assessment of the integrity of DW and also for the detection of potential faulty distribution networks that could constitute a public health hazard.

AIMS AND METHODS: We have taken a new approach for evaluating the integrity of water distribution systems that relies on identifying samples that contain a microbial community that is different from that in the remainder of the distribution network. We base this on the hypothesis that in an intact DW distribution network, microbial succession after treatment will be reasonably predictable. In the absence of allocthonus materials, this development of the authoctonus microbial community will produce only small variations in the microbial community throughout the network. Therefore, an alteration in the overall microbial community might indicate the ingress of exogenous materials and might reflect a potential port for pathogen ingression. If true, such a methodology will enhance the efficiency of detecting health risks associated with DW and potential infectious sources and, will ensure the timely repair of defective networks before they compromise public health. In collaboration with United Utilities, North West England we have access to DW distribution networks that function optimally and those that are defective and offers a possibility of testing our methods in situ. Initial methods development is being conducted on tap water supplied to households in Norwich. Water samples are filtered, DNA extracted and the whole microbial community fingerprinted by PCR-dependent Automated Ribosomal Intergenic Space Analysis (ARISA) using domain specific primers.

PRESENT AND FUTURE: ARISA worked well for whole community profiling of our samples. Current results suggest strong differences in the microbial communities present in kitchen tap water against those present in bathroom tap waters stored in tanks. The archaeae are common in bathroom tap water resampled from three different distant locations but not in kitchen tap waters from the same locations. In some of the bathroom samples, we have discovered gene markers that suggested the presence of the eukaryae. These initial results therefore suggest that the immediate treatment of DW might discourage the survival of the archaeae and eukaryae or that they are reduced to numbers below detection after treatment. We have data that indicates that in all the different tap waters tested ~10^4−10^5 cells l^{-1} are common with ca. <20% representing live cells. These observations therefore tentatively put the archaeae and eukaryae as possible indicators of a compromised distribution network deserving further investigation on a larger scale. Other methods for assessing the microbial communities are currently being tested and include determining domain-specific microbial gene markers in the DW by real time PCR, DNA sequencing and phylogenetic reconstruction.

Multiple environmental classification of areas for researching health inequality

Richard Mitchell[a], Niamh Shortt[b], Jamie Pearce[c], Terry Dawson[d], Elizabeth Richardson[b]

[a] University of Glasgow, UK, [b] University of Edinburgh, UK, [c] University of Canterbury, New Zealand, [d] University of Southampton, UK

BACKGROUND:
There is considerable social and spatial inequality in population health in the UK. Whilst socio-economic deprivation 'explains' (in a statistical sense) much of it, significant proportions of both the variation and its causal mechanisms remain unexplained. Physical environmental factors are thought likely to be significant. In epidemiology, research into population level health inequalities has been greatly aided by indices of multiple deprivation. These indices represent absolute and relative levels of exposure to numerous dimensions of social and economic hardship within small spatially defined populations. However, whilst evidence suggests that both health-promoting and health-damaging components of the physical environment may be implicated in population level health inequality, there is currently no standard means of characterising exposure to health-related multiple environmental deprivation. Such an index could aid efforts to further explain health inequalities, and to focus interventions.

OBJECTIVE:
To create an evidence-based, health-relevant, index of environmental deprivation, and investigate its utility in explaining spatial inequalities in population health. We will pilot the index in the UK and subsequently test its methodology in New Zealand. This is a proof of concept study, from which it is hoped that improvements will stem in the future.

PROGRESS (September 2007 to January 2008)
a. *Identify environmental factors:* A systematic literature search was conducted to select environmental attributes with the greatest potential for affecting population health. The evidence was appraised based on the proportion of the UK population exposed, the prevalence of the health outcome and the strength of association. As a result, we decided to seek datasets concerning air pollution, drinking water quality, radon, solar UV exposure, deviance from comfortable climate and access to greenspace, with the aim of including these factors in the index. Data will also be sought for environmental factors for which the available evidence precluded a rigorous appraisal (noise, industrial facilities and radiation from power lines).

b. *Acquisition of environmental datasets:* We are currently acquiring suitable, available data to capture the selected environmental attributes.

FUTURE WORK (February 2008 to February 2009)
Following acquisition and preliminary processing of the relevant datasets we will

- investigate and select the appropriate spatial scale for the index
- create an index of multiple environmental deprivation
- use the index to investigate the relationship between environmental deprivation, socioeconomic deprivation and selected health outcomes (all cause mortality, cause-specific mortality and self-reported morbidity), in the UK and New Zealand.

Determinants of Oxidative Potential: A Health-Based Metric to Assess Particulate Matter Toxicity

Roy Harrison, Tim Evans, University of Birmingham
Frank Kelly, Chrissi Dunster and Tim Baker, King's College London

Much attention has recently been directed toward identifying the toxic components of particulate matter (PM), which could be used as more precise metrics of its potential toxicity. As PM toxicity is likely to reflect the sum of multiple toxic components we believe approaches focusing on single factors are unlikely to be fruitful. Moreover, we contend that a biologically meaningful measure of PM toxicity that integrates PM composition and size distribution is a more logical strategy, with the long-term aim of establishing a 'biologically-active' PM metric for ambient air. PM oxidative potential is such a possible metric and numerous toxicological studies have documented the capacity of inhaled PM to cause oxidative stress within the lung (Bonvallot, 2001; Mudway, 2004). Therefore a measure of the oxidative potential of PM could provide a health relevant PM indicator that could be more informative than mass alone. In addition, by relating this 'integrative' measure of PM activity with detailed size-segregated chemical analysis of PM samples it should be possible to identify those PM fractions and PM components that contribute significantly to the observed oxidative activity of ambient PM.

To address this issue permission was obtained to undertake a PM sampling campaign in a cohort of seven schools in London that experience a range of traffic flows. The Schools are: Haimo Primary School, Bannockburn Junior & Infants Mixed School, Belvedere Infants School, Holy Family Primary School, Aylward First & Middle School, Blair Peach Primary School and Bowes Primary School. Of importance, each School already has within it boundaries a London air Quality Monitoring site which provides detailed information about air quality in that vicinity. As part of this study additional sampling equipment (Micro-Orifice Uniform Deposit Impactor, Condensation Particle Counter and Epiphaniometer) is being located at each site as part of a PM sampling campaign. The campaign equipment is moved to a new site on a 2-week rotational basis.

The sampling campaign commenced mid-November and will be complete by April 2008. Thereafter we will establish the composition and toxicity of the PM at these sites (PM size fractions; UF, F, and coarse). Composition, (elemental carbon, trace metal and soluble ion content) will be examined in Birmingham and oxidant potential (by antioxidant depletion from lung lining fluid) in London.

On obtaining these data we will determine those PM components associated with increased oxidative potential and address if these are related to the traffic densities/flows at these locations. The work undertaken in this project is viewed as the first stage of a project in which the impact of traffic pollution on children's health at each of these Schools will be examined.

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Born in Bradford: Environmental Exposure and Birth Weight
Nieuwenhuijsen, MJ

A Preliminary Assessment of Levels of Bioavailable Anthropogenic Platinum-Group, Lanthanide and High Field Strength Metals in Human Tissue and DNA

Graham Pearson

The addition of lead substitutes to automotive fuel and the introduction of catalytic converters have led to the appearance of several other, normally rare metals, in exhaust emissions. Over 95% of all cars now manufactured have metal-based two or three-way catalytic converters and emissions from these systems is leading to a well documented, dramatic increase in the concentration of platinum in roadside and tunnel dusts. Little information is available for some of the other rare metals such as cerium, hafnium and zirconium, which can be present in very much higher abundances than Pt in the wash coats of converters, but it is likely that they are accumulating too, probably in much greater abundances. These metals are emitted as ultra-fine reactive particles, and so are readily absorbed when inhaled and consequently are more likely to produce toxicological effects. A chance discovery that at least one of these metals, hafnium, may become incorporated into the primary genetic material (DNA) of some individuals implies that even metals which are usually innocuous can become biologically active if absorbed by the lung in this way. More importantly, this incorporation into DNA implies that they might increase the risk of lung or other cancers by altering or damaging DNA replication. Some of the metals in question (cerium and hafnium) have isotopic compositions that vary in nature and it may be possible to specifically identify the source and sink of these elements in the environment and in the human body through characteristic isotopic compositions that will "fingerprint" their origin. To properly evaluate the risk to human health through accumulation of these metals in the environment we need to instigate a research programme to define basic information such as:-

Is there evidence for accumulation of anthropogenic cerium, hafnium and zirconium consistent with the increase in some platinum group elements?

What are the main environmental sources and pathways of these metals into human receptors and what are the most bioavailable forms?

To what extent do these levels vary between individuals?

To what extent can we distinguish sources using isotope ratio tracing?

What are typical baseline levels of these metals, in human organs such as the lungs and the liver, in human blood and in DNA extracts?

To what extent do the metals become mobilised and biologically active by measurement of the levels bound to DNA and certain proteins

We have assembled a diverse team of scientists with environmental, biomedical, clinical and toxicological expertise that offer a very fortuitous combination of the latest analytical and extraction technology plus access to human tissue and blood samples. This cross-disciplinary team, together with a post-doctoral scientist, will be well pace to answer the above questions and hence provide preliminary data on which to base future studies and risk assessments for human health.

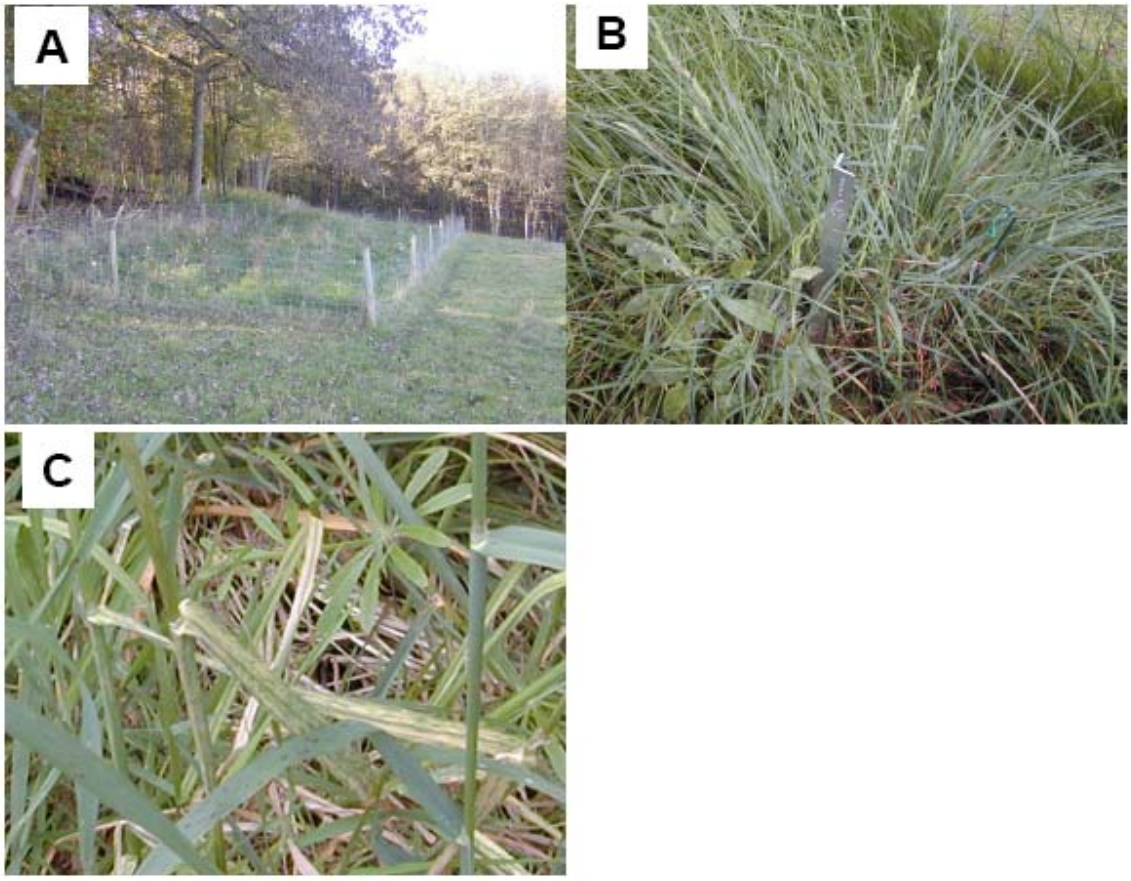
Project due to start in February 2008 when final ethical approval has been processed.

Plant Virus Infection as a Determinant of Pollen Allergenicity

Hui Wang, NERC/CEH-Oxford, Mansfield Road, Oxford OX1 3SR

This project is funded by E&HH in conjunction with NE/E009417/1 to Dr. Andrew Walls in the University of Southampton. We started the CEH project on 1st Oct 2007, aiming to harvest grass pollens in spring-summer 2008.

● A number of *Cocksfoot streak virus* (CSV) infected wild perennial grasses have been identified in the Great Wytham Wood, Oxfordshire.
● Cocksfoot (*Dactylis glomerata*) lines with CSV and *Cocksfoot mottle virus* infections, and sweet vernal grass (*Anthoxanthum odoratum*) lines with *Anthoxanthum latent blanching virus* infections are being established by tiller propagation.
● Infected/un-infected grasses will be tested individually for presence/absence of viral proteins or nucleotide acids, before pollen harvesting.



A: Study site in Wytham Wood, Oxford.
B. Individual grasses are labelled.
C. Symptoms can be observed from some individuals. Protein (ELISA) or nucleotide acid (RT-PCR) tests of leaf extracts confirmed infections of *Cocksfoot streak virus*.

Modelling and Measurement of Cadmium Exposure and Pathology in Human Volunteers Living in Proximity to a Smelter Source

Dave Spurgeon, Claus Svendsen - Centre for Ecology and Hydrology, Monks Wood
Jake Bundy, Hector Keun, Jim Ellis - Division of Surgery, Oncology, Reproductive Biology and Anaesthetics, Imperial College, London
Lars Jarup, Laura Thomas - Division of Epidemiology, Public Health and Primary Care, Imperial College, London

Among pollutants, toxic metals and metalloids offer one of the greatest risks to the health of humans and ecological species. Measurement and modelling studies have established that there are many areas of the UK where soil concentrations of metals and metalloids such as arsenic, cadmium, copper, mercury, lead and zinc exceed the environmental quality standards that are indeed to protect the health of the general public and ecosystems. As the biological half-life of Cd in humans is very long, extended exposure to this metal results in an increase in concentrations of this metal in sensitive organs. Such accumulation is associated with an increase in the probability of adverse health problems including effects on the function of major organs such as the liver and (of particular relevance to this project) kidney. Bone disease and cancer are also known to be prevalent in Cd exposed populations. In this exploratory study, we seek to improve our capacity to define the link between the concentration of Cd in the environment (air, soil, water, food), the extent of human exposure and the potential for resulting health effects. This will be achieved by adding field measurements of metal concentration, exposure modelling studies, exposure monitoring by Cd measurement and new metabonomic based health assessment technologies to an ongoing human volunteer study focused on a polluted area. Specifically in the work funded within the NERC Environment and Human Health program we are:

- measuring current environmental Cd concentrations around the study site in soils, air, house dust for application within and validation of human exposure assessment models such as the EA CLEA and Dutch NormTox models;
- modelling plant uptake of Cd using a free ion based approach that includes parameters to account for the impacts of competing ions (e.g. H^+) and undertaking a validation to allow prediction of exposure through home grown vegetables;
- using a metabonomic approach to investigate human volunteer urine samples for metabolic dysfunction, augmenting classic renal dysfunction and Cd measurements;
- and using classification based algorithms to ascribe change in markers of organ pathology to environmental exposure assessments and urinary measurements and establish correlations between human effects and environmental impacts.

The program of research will provide new geospatially-referenced database directly relevant to assessing cadmium exposure and effects in the human, as well as provide a “proof-of-principle” experiment for the use of metabonomics in human population toxicology. The measurement and modelling strategy optimized will also be of value for future prediction of cadmium (and other heavy metal) risks to human health associated with past and present release. The data on human exposure assessment will also be compared to results from previous studies on the ecological effects of the pollutants present at the same site. Such integrated analysis of the consequences of chemical exposure for both human and wildlife is an emerging field and this study will be among the very first to start to address the issue of exposure effect coincidence between ecological species and humans.

Seasonal Environmental Hazards: A Multi-disciplinary Approach to the Analysis of Health Risks in Lower-income Countries

Roger Few/Paul Hunter/Iain Lake, University of East Anglia, UK
Pham Gia Tran, University of Social Sciences and Humanities, HCMC, Vietnam
Vu Trong Thien, Institute of Hygiene and Public Health, HCMC, Vietnam

July 2007 - September 2008

This project involves field testing of a streamlined multi-disciplinary approach to the analysis of risks to human health from seasonal environmental hazards in developing countries. The research is taking place in Vietnam: in four areas of the city of Long Xuyen in the heart of the Mekong Delta. Each year these sites face alternate seasonal extremes in the local environment, as the water level in the Mekong Delta changes from flood to dry season. For poorer households in particular, the potential health consequences of these environmental cycles are considerable. Such households tend to rely heavily on river water for domestic uses including provision of drinking water, and it is commonly perceived that the seasonal changes alter risk from diarrhoeal diseases and other diseases associated with contamination of water. Following fine-tuning and piloting of the research methods in the field, two out of three phases of data collection are now complete (flood season and interim phase), and analysis of data from the first phase is under way.

The research is generating an integrated dataset combining information from environmental monitoring, health data and analysis of health behaviour. It entails:
a) Environmental monitoring for microbial risk
• Microbiological environmental sampling designed to determine the potential exposure of residents to faecal pollution within the home and the immediate surroundings, and gauge how this changes on a seasonal basis. During each of three seasonal research phases the team is taking samples of stored water sources from 120 households (30 per site). Each sample is being analysed for Total coliform and E. coli using portable equipment (IDEXX Quanti-Tray system).
b) Analysis of public health data
• Monthly data on health outcomes is being compiled from health clinic records for the period 2002-2008 (plus corresponding river height and rainfall data).
• During each research phase population surveys are being conducted with the same 120 households as above to identify the community incidence of self-reported diarrhoea and other infections plus information on a range of risk factors.
c) Household-level research on health behaviour
• During the first research phase, a questionnaire survey on health behaviour was carried out with the 120 households, gathering data on perceptions of health risks and how risk change during the seasons, hygiene practices, specific responses to the health risks from floods, and reasons for practices.
• During the third research phase, a follow-up process of 32 semi-structured interviews (8 per site) will be carried out with a stratified sample of respondents to gain more intensive, qualitative information on how perceptions, motives and constraints shape health protection behaviour.

Helminths as Vectors of Food-borne Pathogenic Bacteria in the Environment

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[1]University of the West of England, Bristol, UK [2]Center for Infectious Disease Dynamics, Penn State University, Pennsylvania, USA, [3] University of Bristol, Bristol, UK

Food-borne diseases are a significant public health problem. Pathogens, such *Salmonella*, can be found in the soil where they interact with other organisms, including microbiovorous helminths, which use bacteria as a source of nourishment. *Salmonella* can survive and proliferate in the gut of helminths and viable bacteria are shed into the environment by infected helminths. Therefore free-living and parasitic helminths could provide an important and under-studied mechanism by which pathogens could persist in the environment and be transmitted to humans.

We are investigating whether helminth vectors confer advantages to pathogenic bacteria that may increase their fitness and their ability to persist and transmit in the environment. Our project is divided into three parts, to establish:
1. whether carriage within helminths confers an advantage to bacterial pathogens under different environmental conditions
2. whether helminth carriage increases bacterial infection of a vertebrate host (mice) using *in vivo* real-time imaging systems
3. whether there is differential gene expression of the pathogen inside the helminth gut.

A novel monitoring system using bioluminescent reporter bacteria was employed to study the pathogen - helminth interaction. Genetically modified *Salmonella* that constitutively express the *lux* genes (*S. enterica* serovar Typhimurium DT104 *pGLITE*), and therefore are bioluminescent, were used to monitor the survival, growth and transmission of the pathogen *in-vivo* and in real time, by measuring bacterial light output. As a model for helminth the free-living soil nematode *Caenorhabditis elegans* was used.

In our investigations of pathogen persistence and survival we have found that *C. elegans* offered protection to the bacteria under harsh environmental conditions. We have determined that *Salmonella* ingested by *C. elegans* survives at a range of pH values and disinfectant treatments compared to *Salmonella* alone, when exposed to the same conditions (Fig. 1). We find, also, that *Salmonella* survives for a longer time period in soil when *C. elegans* are present. Increased bioluminescence over a longer time interval was observed in the presence of *C. elegans*, indicating that nematodes may potentially increase persistence of *Salmonella* in the soil (Fig. 2). These results have substantial implications for the control of bacterial infections in the environment.

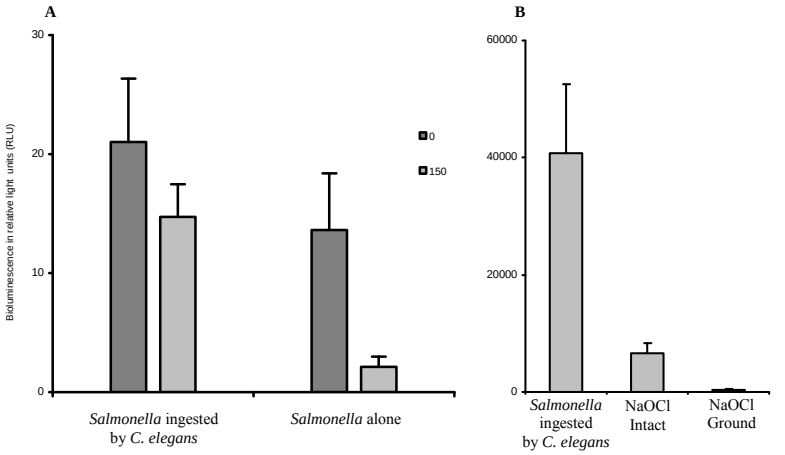

Fig 1. Bacterial survival under harsh environmental conditions. (a), exposed to a pH 2.0 solution (comparing *t*= 0 and *t*= 150); (b) exposed to NaOCl inside helminth gut (intact *C. elegans*) or free (ground *C. elegans*).

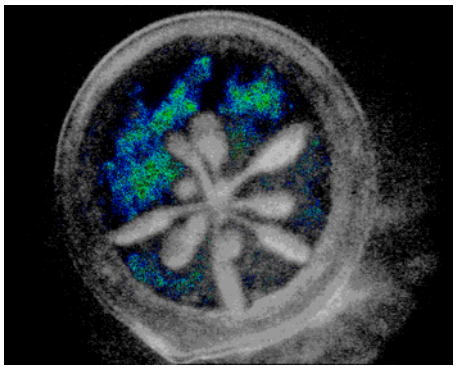

Fig 2. Bacterial persistence in soil in presence of nematodes. Image of soil with Arabidopsis plant infected with bioluminescent *Salmonella*.

Hazards of Nanoparticles to the Environment and Human Health

D. Berhanu [(1)], A.R. Boccaccini[(2)], T. D. Tetley[(3)], J. Plant[(4)], E. Valsami-Jones[(1)]
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Nanoparticles are very small entities of 100nm and below. Their size is intermediate between bulk and molecular dimensions which confers very particular properties that are different from the corresponding bulk materials. Offering new perspectives, from materials science to medicine, textiles and electronics, their predicted applications in the coming years is driving an exponential interest in diverse fields.

Naturally present on earth, human action is increasing nanoparticle concentration in the biosphere by direct (engineered) and indirect (pollution) means and is also creating new nanomaterials with novel properties. The reactivity of nanoparticles is predicted to be much higher than the corresponding bulk materials, perhaps as a result of their different material properties and increased surface area. Consequently, the effect of their presence in the environment at short and long term has to be addressed. Furthermore, the nanoscale corresponds to the smallest compounds in human bodies such as organelles or proteins, and the reactivity of nanoparticles once in the body is virtually unknown. However, this needs to be investigated urgently as many more products are becoming commercially available (www.nanotechproject.org/consumerproducts) without putting parallel controlling and/or assessment systems in place.

This project aims to investigate the link between physicochemical properties of nanoparticles and their reactivity in vitro. The behaviour of two types of common engineered nanomaterials, multi-walled carbon nanotubes and titania nanoparticles, will be studied in simulated lung and body fluids. These will provide models for the first sites of reactivity following deposition of inhaled particles in lung secretions and the effects of inhaled nanoparticles on the cardiovascular system of humans respectively. Our working hypothesis is that nanoparticle reactivity can be specifically linked to one or more of:

- Their physicochemical properties, specifically, size, shape, structure, composition, surface modification and form of delivery (i.e. free vs. attached);
- Their environment (in terms of temperature, pH, Eh, chemical composition and in the case of photosensitive nanoparticles such as titania, light).

We will be presenting preliminary results from the evolution of physicochemical properties of TiO_2 nanoparticles in different media

Model Human Digestive System for the Determination of Bioaccessibility of Environmental Pollutants.
Gibson, GR

Strategies to Manage Toxic Cyanobacterial Blooms in Lakes: Remote Sensing, Modelling and Cost-Benefit Analysis

Andrew Tyler[1*], Laurence Carvalho[2], Geoffrey Codd[3], Alex Elliot[4], Claire Ferguson[5], Nick Hanley[6], David Hopkins[7], Peter Hunter[1], Stephen Maberly[4], Marion Scott[5] & Michael Wyman[1]

[1]*School of Biological and Environmental Science, University of Stirling*; [2]*Centre for Ecology and Hydrology, Edinburgh*; [3]*Division of Environmental and Applied Biology, University of Dundee*; [4]*Centre for Ecology and Hydrology*, *Lancaster Environment Centre*; [5]*Department of Statistics, University of Glasgow*; [6]*Department of Economics*, *University of Stirling*; [7]*Scottish Crop Research Institute, Dundee*. *Principle Investigator.

Overview and Progress

Cyanobacteria are natural inhabitants of fresh-, brackish- and marine waters. However, the development of mass populations of cyanobacteria can present a significant risk to human and animal health because of their capacity to produce numerous potent toxins. This multi-interdisciplinary project aims to develop novel strategic tools to improve the monitoring and management of potentially-toxic cyanobacteria blooms in lakes using the approaches outlined below.

(1) General additive models for cyanobacterial hazard assessment have been developed using data from 134 UK lakes and used to explore relationships between the occurrence of commonly recorded potentially-toxic and bloom-forming cyanobacteria and explanatory environmental variables (e.g., nutrients, alkalinity, water colour, temperature, lake area, lake depth). These results will be used to further develop models for predicting the risk of developing blooms of potentially-toxic cyanobacteria in UK lakes.

(2) The process-based PROTECH (Phytoplankton RespOnses To Environmental CHange) model is being used to examine the effect of future climate changes on the occurrence of cyanobacteria blooms in lakes. Model scenarios are currently being developed for Esthwaite Water under different future temperature and nutrient loading regimes.

(3) The potential of remote sensing to provide an early-warning surveillance capability for cyanobacterial bloom development in lakes is being investigated using data acquired by the NERC Airborne Survey and Research Facility. Algorithms for the estimation of chlorophyll-a and the biomarker pigment C-phycocyanin in cyanobacterial blooms are being developed and validated in two UK lakes (Esthwaite Water and Loch Leven). This data will be used in conjunction with estimates of cyanobacterial biovolume and toxin concentrations to more accurately determine the limits of detection of the remote sensing approach for cyanobacterial bloom monitoring.

(4) The dynamics of microcystin gene expression and production in cyanobacterial blooms is being investigated in natural populations through quantitative RT-PCR and the data are being related to seasonal changes in the abundance of toxic genotypes through DGGE and sequence analysis of the *mcyA* gene. These analyses will be correlated against cyanotoxin and physico-chemical data to provide new insights into the environmental regulation of toxin production.

(5) A small-scale socio-economic survey of recreational users of Loch Leven has been conducted to investigate public perceptions of water quality in the loch. It was found that 80% of respondents expressed a willingness to pay for water quality improvements, while the same improvement would cause 25% of respondents to increase the frequency of future visits. It is anticipated that this survey will be extended to examine the responses of other user groups (i.e., anglers and local residents) to changes in water quality in Loch Leven. In addition, a further survey will use risk ladders to examine the relationship between the perceived and measured risk from potentially-toxic cyanobacteria blooms.

Exploring the Link between Surface Structures and Toxicity in Mineral Particles: Case Study of Induced and Intrinsic Toxicity in Quartz
Ed Stephens, St Andrews University & CoIs

Crystallographic characterisation of representative industrial quartz materials indicates that the degree of lattice strain is highly variable, as reflected in the peak broadening effect shown in Fig.1. DQ12, the most toxic of all quartz powders used in toxicological experiments, is highly strained compared with a reference euhedral quartz of minimal strain (ACEQ) whereas Min-U-Sil 5, also widely used in toxicology, has intermediate strain. The hypothesis that variable amounts of strain could be irreversibly induced in quartz, mimicking mechanical damage induced by mining/quarrying operations has been tested using a range of methods. Successful replication of strain broadening patterns was achieved by grinding a low strain quartz crystal in a ball mill for different periods of time (Fig.2) and this effect survives annealing at 500°C for 48 hours. Lattice strain is estimated using a fundamental parameters spectral modelling approach.

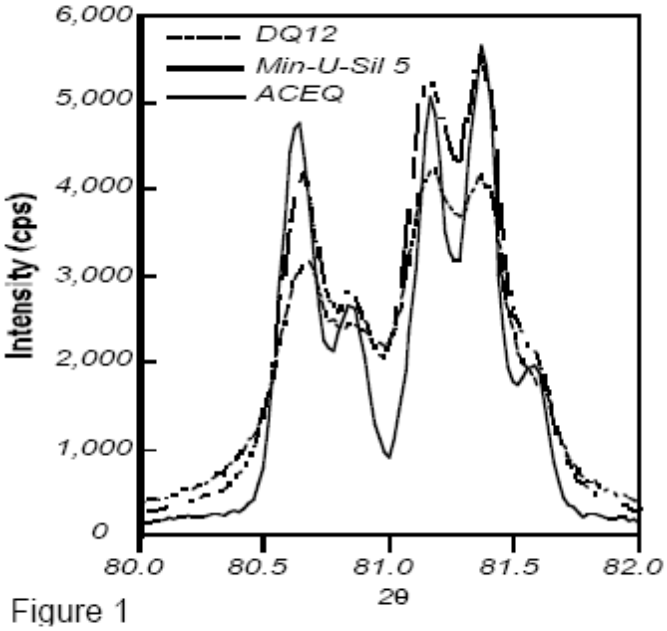


Figure 1

An outcome of these experiments is a unique suite of quartz powders of variable strain that share the same compositional and grain size characteristics. With strain as the only major variable these samples are currently being characterised for surface functional groups, especially silanol density using FTIR; XPS and desorption mass spectrometry will follow shortly. At the same time a group of standard quartz powders including DQ12 and Min-U-Sil 5 are being similarly characterised. The same samples will be subject to measurement of IL-8 and lactate dehydrogenase (LDH – a protein indicative of cell damage) in human lung epithelial cells as well as red blood cell haemolysis (a test of the ability of the particles to cause membrane damage), which have been used extensively in particle toxicology as short term predictors of toxicity *in vivo*. Comparing these toxicological results with the measures of strain already obtained will allow us to test the hypothesis that induction of strain contributes to the toxic effects of quartz.

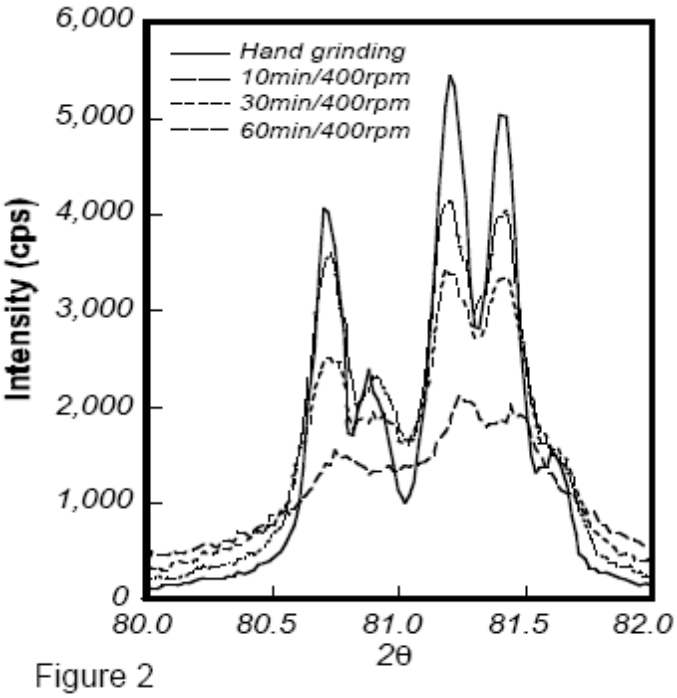


Figure 2

Nanotoxicology of Fine PM

Dr Michaela Kendall[1], Dr Ping Ding[1], Prof Kevin Kendall[1] and Prof Howard Clark[2]
[1]Birmingham and [2]Southampton Universities, UK

Evidence from two methodological approaches – epidemiology and toxicology – has shown detrimental health changes in response to atmospheric exposures to fine and nano-sized particulate matter (PM; Pope and Dockery, 1999). Implicated PM characteristics include surface area, particle composition and nanoparticles (Oberdorster et al., 1994; Johnston et al., 2000; Peters et al, 1997). Nanoparticles are able to access the lower lung in greater quantities than larger particles. In the alveolar spaces, these particles initially impact on the surfactant lung lining liquid layer. This layer enables oxygen exchange, lung expansion and also provides primary host defence against depositing foreign material, such as solid and biological particles.

We are testing the hypothesis that opsonisation of depositing PM in the lung alters to the function of lung through the sequestration of defensive proteins and lipids from the lung lining fluid. This process may be as important for labelling and collection for solid particles as they are for biological particles. Sequestration of biomolecules from the lung lining by PM surfaces is expected to result from this adsorption, which may have significant health consequences where large surface areas are deposited. Since the coating of deposited PM by host proteins may modulate their biological activity, as they do for infectious particles, studies of such interactions will provide new information as to how inhaled pollutants may induce pulmonary and cardiovascular toxicity.

To date we have selected a series of particles to characterise in our laboratories, and use in a series of experiments with lung surfactant components. We have characterised the size distribution and surface character of hydrophobic and hydrophilic silica, carbon black, and 8 types of polystyrene particles within the 100-200 nm size range. Baseline studies of these particles are complete. We have furthermore selected 3 lung proteins and 1 lung surfactant lipid to test in aggregation experiments with these particles. We have established test procedures for measuring changes in PM-protein/lipid systems. Light scattering techniques will provide the best definition of size distribution changes, while optical microscopy will confirm the orientation and density of aggregates. TEM will provide a sensitive measure of how particle surface chemistry affects initial aggregation of agglomerates.

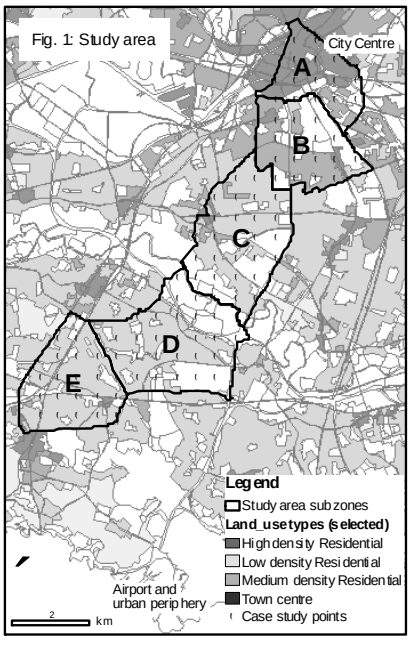
Identification and Verification of Ultrafine Particle Affinity Zones in Urban Neighbourhoods

Paul Harris[1], Sarah Lindley[1], Anna Leavey[2], Raymond Agius[3] & Martin Gallagher[2]
[1]*School of Environment & Development (Geography).* [2] *Centre for Atmospheric Science, School of Earth, Atmospheric & Environmental Science.* [3]*School of Occupational & Environmental Health. University of Manchester.*

Context There is currently a great deal of concern that fine particles (PM_{10}, <10mm) have an as yet unquantifiable but adverse effect on human health in urban areas. Toxicological investigations have suggested that ultrafine particles (UFP, <100nm), largely derived from combustion, are more toxic per unit mass than larger particles[3]. Further assessment of the relationships between UFP metrics, such as particle numbers and health effects in the general populace is urgently required, but is currently prevented by our inability to provide appropriate exposure assessment. Compared to PM_{10}, number concentrations of UFP are subject to a much greater spatial variability and strong metre-scale gradients, especially in cities. This cannot be captured explicitly by conventional low density monitoring networks. Furthermore, human populations are highly mobile within these concentration fields, necessitating development of improved techniques for understanding patterns of exposure and their relationship with underlying indicators of behaviour & health.

The Problem There are no protocols for selection of appropriate measurement sites for the purposes of UFP exposure studies. To further investigate the effects of UFP on health it will be necessary to generate UFP exposure data for large populations and develop techniques to use fixed point data to represent a wider neighbourhood. Large spatial gradients in UFP concentrations are caused by spatial variability in a number of factors, including emission source types and strengths, factors affecting dispersion and particle removal mechanisms such as deposition. This pilot study is investigating these geographical influences with the contention that they can be quantified and processed using Geographical Information Science. A further aim is to assess the optimal location requirements of fixed UFP monitor sites so that the represented area and exposed population can be quantified in a robust way. This will allow:

- comparison of UFP concentrations with other metrics
- tests of the spatial representativeness of existing monitors
- development of a basis for long term monitoring protocols of UFP for epidemiological studies.



Progress to date Field activities started in January 2008 with siting of the fixed monitors and the initiation of spatial sampling. Sampling will be carried out over the winter and summer periods to capture seasonal variations The spatial sampling strategy is targeted within an initial case study area of approximately 30km^2 (Fig 1). The SW-NE transect contains 224 polygons and 22 land-use types associated with differing surface covers, source types and exposure characteristics. A geospatial database of covariates is under construction to underpin model development. The aim of the model is to characterise environmental exposure for UFPs and relate those findings to existing cohorts. The results will be ideally suited to describe the outdoor concentrations at residential and workplace locations, but will also inform further studies on commuting and pedestrian activity and exposure.

[3] Oberdorster, G., 2001, Intl Arch Occup Env. Health 74(1)