Workshop on Statistical Systems Biology
9th – 11th December 2014
University of Warwick

Organising Committee: Mark Girolami, Chris Oates, David Rand (Warwick)

The workshop proceedings are due to be published in Statistical Applications in Genetics and Molecular Biology (SAGMB; De Gruyter), anticipated early 2015 (pending revisions). The organisers wish to thank Michael Stumpf, Editor of SAGMB, for his willing engagement and assistance in this process.

Contents

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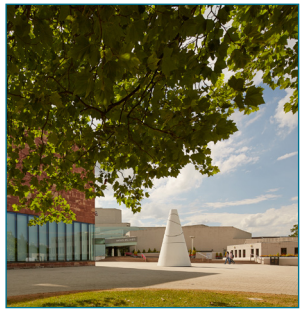
SYMBOLS

- University Buildings
- Student Residences
- Car Parks
- Building Entrances
- Wheelchair Access
- Controlled Access
- Footpaths
- Footpaths/Cycleways
- One way Road
- Bus Stop
- No Entry
- Lakes
- Food Outlets

Important Postcode Information

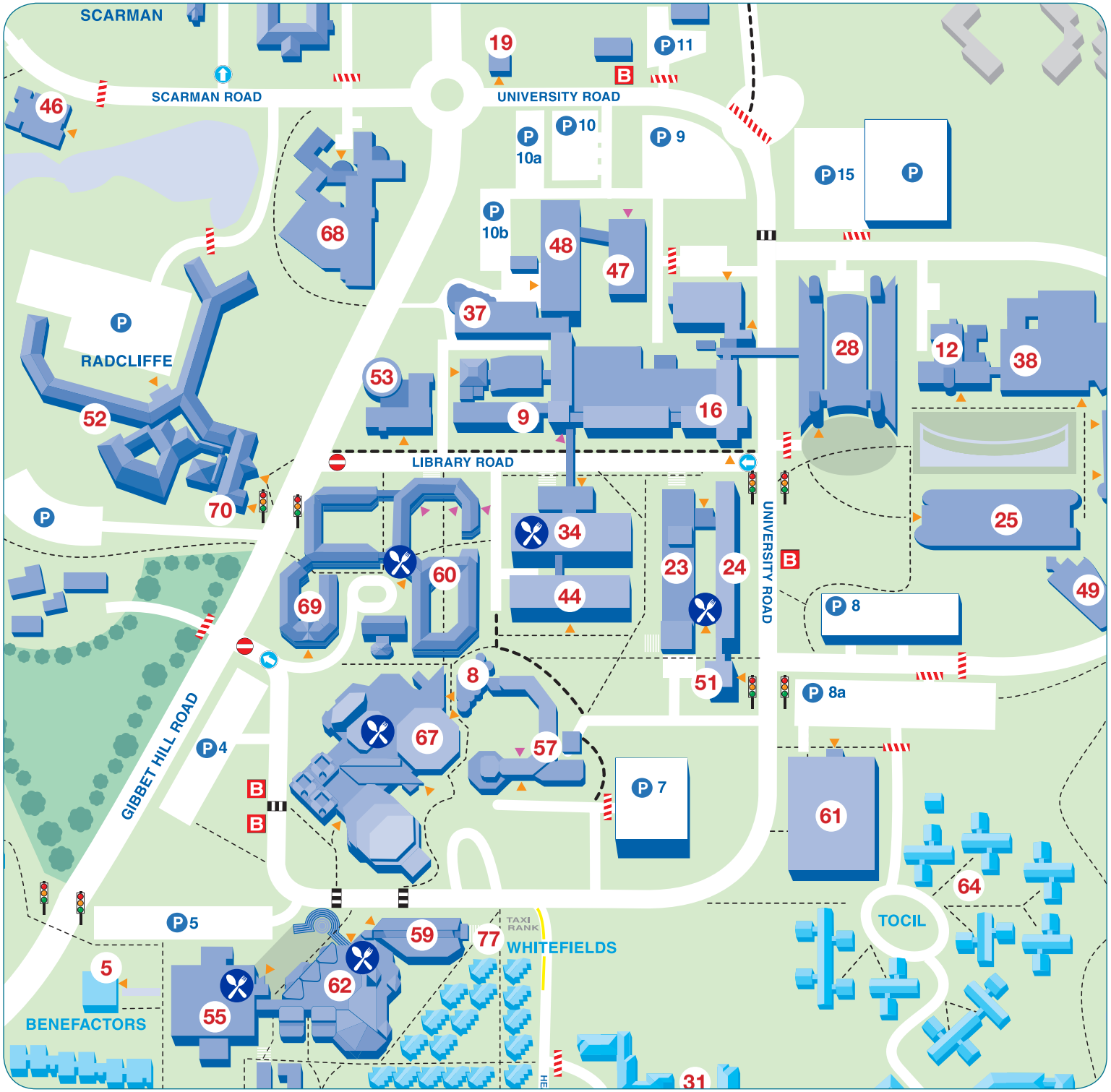
CV4 7AL directs you to Gibbet Hill Road, the main road which runs through the University. Radcliffe, Scarman and main campus (the Conference Park) are signposted from this road.

CV4 8UW directs you to Kirby Corner Road where Arden is signposted.



67. Warwick Arts Centre

62. New Conference Reception for 2014



23. Humanities

Building Key

1 Administrative Details

1.1 Conference Webpages

- http://warwick.ac.uk/SSB

1.2 Registration and Venue

- **Registration:** 09:00-09:30, Tue. 9th Dec., Maths & Stats Building, Lobby.
- **Talks:** Maths & Stats Building, [MS.05 Tue. and Wed.] [MS.02 Thurs.].
- **Poster Session & Wine Reception:** 16.40-18.00, Tue. 9th Dec., Maths & Stats Building, Lobby.
- **Breakfast (Tue., Wed., Thurs.):** 7.30-9am, Rootes Social Building. [Participants with on-campus accommodation only]
- **Lunch (Tue., Wed., Thurs.):** 12.40-13.40, Maths & Stats Building, Lobby.
- **Conference Dinner (Wed.):** 19.30, Rootes Social Building (Chancellors Suite).
- **Conclusion:** 15:00, Thurs. 11th December.

1.3 Getting Here

- Information on getting to the University of Warwick from Coventry, as well as from other directions locally and further afield, can be found at http://www.warwick.ac.uk/about/visiting/

1.4 Accommodation

- Accommodation is in en-suite rooms on campus in the Jack Martin residences (see the campus map). For keynote speakers, accommodation is instead in en-suite rooms on campus in the Radcliffe residences (see the campus map).
- Keys can be collected from the Conference Reception in the Student Union Atrium. All rooms have linen and toiletries. Kitchen facilities may be available although meals are provided throughout the workshop.
- Please find further information in the Appendix of this booklet. Rooms will be available after 15:00 for check in. All bedrooms must be vacated by 9:30am on the day of departure.

1.5 Internet Access

- **Campus:** Wireless access is most easily available via eduroam — http://www.eduroam.org/ — which is supported across most of the Warwick campus. Speak to one of the organisers for details of other options.
- **Accommodation:** Wireless access is available, ask for log-in details whenever you check-in to your accommodation.

1.6 Start.Warwick

- The Start.Warwick app (available for iPads, iPhones and Android devices) provides useful information on travel and an interactive map of the campus amongst other things.

1.7 Facilities - See Map

- **Supermarket, Food and Drink Outlets:** `http://www.warwickretail.com`
  - See Appendix for opening times.
- **Arts Centre:** `http://www.warwickartscentre.co.uk`
- **Sports Centre:** `http://www.warwick.ac.uk/sport/`
- **Health Centre:** `http://www.uwhc.org.uk`
- **Pharmacy:** Students Union Atrium

2 Help, Information & Telephone Numbers

2.1 Department

- **Address:** Department of Statistics, University of Warwick, Gibbet Hill Road, Coventry, CV4 7AL
- **Telephone:** 024 7652 4553
- **Fax:** 024 7652 4532
- **Webpage:** `http://www.warwick.ac.uk/stats`

2.2 Emergency Numbers

- **Emergency:** Internal - 22222; External - 024 7652 2222
- **Security:** Internal - 22083; External - 024 7652 2083
- **Organiser:** Internal - 73436; External - 024 7617 3436 (Murray Pollock)

2.3 Transport

- **Swift Taxis (Coventry):** 024 7676 7676
- **Trinity Street Taxis:** 024 7699 9999
- **National Rail Enquiries:** 08457 484 950

3 Timetable

All activities will take place in the Mathematics & Statistics Building, with talks on Tue. 9th and Wed. 10th in room MS.05 and talks on Thurs. 11th in room MS.02 (signposted from lobby).

3.1 Tuesday 9th December

Time	Speaker	Title	Pg
09:00	**Registration**	*In "the street"*	**-**
	Chair: Chris Oates		
09:30	David Rand [⋆]	Systems Biology and some of its statistical challenges: the view from Warwick	9
10:30	**Coffee break**	*In "the street"*	**-**
	Chair: Simone Tiberi		
10:50	Bärbel Finkenstädt	Switch time modeling for gene expression: An overview	9
11:15	Kirsty Hey	Switch time modelling for gene expression: The stochastic formulation	9
11:40	Mustafa Khammash [⋆]	Feedback Control of Living Cells in Noisy Environments	10
12:40	**Lunch**	*In "the street"*	**-**
	Chair: Chris Penfold		
13:40	Ann Babtie	Topological sensitivity analysis for systems biology	10
14:05	Walter Kolch [⋆]	The art of uncertainty and craft of probability applied to the reconstruction of biological networks	11
15:05	**Coffee break**	*In "the street"*	**-**
	Chair: Rich Savage		
15:25	Paddy Slator	Inferring switching diffusion in noisy single particle tracking data	11
15:50	Zoulikha Zaidi	Understanding drug behaviour and signalling molecules interactions through the use of a modified EM algorithm for a sparse structure	12
16:15	Catherine Higham	New Tools for Model Selection in Gene Regulatory Networks	12
16:40	**Poster Session**	*In "the street". Wine and light refreshments will be provided*	21

3.2 Wednesday 10th December

Time	Speaker	Title	Pg
09:00	**Registration**	*In "the street"*	**-**
	Chair: Kirsty Hey		
09:30	Nigel Burroughs [⋆]	Reverse engineering chromosome oscillations	13
10:30	**Coffee break**	*In "the street"*	**-**
	Chair: Steven Hill		
10:50	Saverio Ranciati [○]	Spatio-Temporal Model for Multiple Chip-SEQ Experiments	13
11:15	Veronica Vinciotti [○]	Model selection for dynamic regulatory networks under l1 penalty and structural constraints	14
11:40	Sach Mukherjee [⋆]	Towards empirical assessment of causal inference	14
12:40	**Lunch**	*In "the street"*	**-**
	Chair: Nigel Burroughs		
13:40	Steven Hill	Data-driven inference of causal molecular networks and systematic assessment of inference performance	15
14:05	John Lygeros [⋆]	Estimation and control of cell populations	15
15:05	**Coffee break**	*In "the street"*	**-**
	Chair: David Wild		
15:25	Silvia Calderazzo	Modelling transcriptional regulation of circadian genes of the Arabidopsis Thaliana	16
15:50	Séverine Affeldt	Robust Reconstruction of Causal Graphical Models from Genomic Data	16
19:30	**Conference dinner**	*Rootes Social Building, Chancellor's Suite*	**-**

3.3 Thursday 11th December

Time	Speaker	Title	Pg
09:00	**Registration**	*In "the street"*	**-**
	Chair: David Rand		
09:30	Ramon Grima [⋆]	A comparison of approximation methods for stochastic biochemical networks	17
10:30	**Coffee break**	*In "the street"*	**-**
	Chair: Anne-Marie Lyne		
10:50	Osvaldo Anacleto	Incorporating contemporaneous relationships among gene expression time series into the model selection of gene networks	17
11:15	Chris Oates	Joint Estimation of Multiple Related Biological Networks	18
11:40	Darren Wilkinson [⋆]	Stochastic Modelling of Genetic Interaction in Budding Yeast	18
12:40	**Lunch**	*In "the street"*	**-**
	Chair: Bärbel Finkenstädt		
13:40	Jamie Owen [○]	Likelihood free inference for Markov processes: a comparison	19
14:05	Andrew Golightly [○]	Bayesian inference for Markov jump processes with informative observations	19
14:30	Colin Gillespie [○]	Diagnostics for assessing the accuracy of approximate stochastic simulators	20
15:00	**Concluding remarks**	**-**	-

[⋆] = Keynote Speaker [○] = Highlight Talk

"Highlight" talks represent original work submitted for publication in the SSB proceedings.

4 Talk Abstracts

Systems Biology and some of its statistical challenges: the view from Warwick [⋆]

Prof. David Rand
Director of the Systems Biology Centre, University of Warwick

I will discuss a range of biological and biomedical problems which raise statistical challenges with an emphasis on projects of interest to Warwick researchers.

Switch time modeling for gene expression: An overview

Bärbel Finkenstädt, Dafyd Jenkins, Kirsty Hey, George Minas, David Rand
University of Warwick

Time series relating to gene expression are now routinely measured in various important biological experiments such as microarrays, nanostring, etc as well as experiments based on bioluminescent imaging. One of the most important aim is to gain an understanding of the transcriptional regulation of genes, i.e. what determines their activation. A natural model is to assume that gene activation is a constant rate birth process but that the rate may change to different levels at unknown time points leading to the piecewise linear switch model. Statistical inference for such a model poses interesting and challenging problems, in particular since experiments can only measure events downstream whereas the processes of interest remain unobserved. We will give an overview of our experience with fitting such switch models to real data where, depending on the type of experiment, our assumptions range from stochastic differential equations to the use of ordinary differential equations, along with realistic stochastic formulations of the measurement processes. We will also present further results on extending this nonlinear approach to the multivariate case of identifying networks of interacting genes. Here we find that the concept of thresholding constitutes a simple yet realistic and very effective modelling device to help identifying network connections.

Switch time modelling for gene expression: The stochastic formulation

Kirsty Hey, Hiroshi Momiji, David Rand, Bärbel Finkenstädt
University of Warwick

Gene expression is made up of inherently stochastic processes within single cells and can be modelled through stochastic reaction networks (SRNs). In particular, SRNs capture the features of intrinsic variability arising from intracellular biochemical processes which when embedded within a hierarchical framework can also account for extrinsic variation. We extend current models for gene expression to allow the transcriptional process within an SRN to follow a random step function, which may be estimated using reversible jump MCMC. This stochastic switch model provides a generic framework to capture many different features of gene expression. However, inference for SRNs is computationally demanding due to the intractability of the transition densities. We will show how state space models provide a unifying framework for approximating SRNs with particular attention given to the linear noise approximation which we compare to an alternative model specific birth-death approximation. Coupling these approximations with a realistic measurement equation enables us to apply our methodology to single cell imaging data measuring expression of the human Prolactin gene.

Feedback Control of Living Cells in Noisy Environments [⋆]

Prof. Mustafa Khammash
Control Theory and Systems Biology, ETH Zurich

Norbert Wieners 1948 Cybernetics presented a vision unifying the study of control and communication in the animal and the machine. Predating the discovery of the structure of DNA and the ensuing molecular biology revolution, applications in the life sciences at the time were limited. Today, the confluence of modern genetic manipulation techniques, powerful measurement technologies, and advanced analysis methods is enabling a new area of research in which systems and control notions are used for regulating cellular processes at the gene level. This presentation describes new analytical and experimental work that demonstrates how de novo control systems can be interfaced with living cells and used to control their dynamic behavior. The feedback systems can either be realised on a computer (in-silico control) using optogenetics or through genetically encoded parts (in-vivo control). Applications in biotechnology and therapeutics will be described. Finally, a new theory for the integral control of stochastic networks is presented and discussed.

Topological sensitivity analysis for systems biology

Ann Babtie, Michael Stumpf, Paul Kirk
Imperial College London and University of Oxford

ODE models are widely used to study the dynamics of biological systems but, by necessity, are abstractions of much more complex processes. To gain meaningful insights into the real system it's essential to understand the impact of assumptions made in a chosen model on our conclusions. We propose a method, topological sensitivity analysis, to assess how uncertainty about model structure influences parameter inference results. Parameter uncertainty is often estimated using methods that condition upon a single specific model, e.g. Bayesian analysis or bootstrapping, while ignoring the contribution of structural uncertainty. We show this may be misleading when we cannot feasibly model the true system complexity. Using synthetic and experimental datasets, we illustrate how we can evaluate potentially vast sets of candidate ODE models to identify those with consistent dynamics, and use these to test the sensitivity of parameter inference results to altered model topology. We find even minor structural uncertainty renders some conclusions unreliable, while other inferences are robust across diverse model structures. Considering the sensitivity of model behaviour to both parameter and structural variation allows us to identify inferences that are robust to potential (and often unavoidable) errors in our model, and thus gain confidence in our conclusions.

The art of uncertainty and craft of probability applied to the reconstruction of biological networks [⋆]

Prof. Walter Kolch

Director of Systems Biology Ireland and Director of the Conway Institute, University College Dublin

Signal transduction pathways mediate the pathogenetic effects of many mutations, in particular in cancer. However, we know very little how genetic mutations play out on the functional level of signal transduction networks. In order to address this bottleneck and harness network information for enhanced patient stratification we will need to (i) develop methods for the integration of different omics technologies that can capture how the effect of a genetic mutation percolates through biochemical and transcriptional networks; and (ii) link alterations in signal transduction pathways to biological and clinical outcomes that enable us to develop prognostic models for patient specific disease outcomes. I will discuss these concepts using examples some of our recent work concerning (i) the integration of Ras network signalling on the interactome, phosphorylation and transcriptional level; and (ii) the use of biochemical pathway models to derive patient specific models for individual disease prognosis.

Inferring switching diffusion in noisy single particle tracking data

Paddy Slator, Nigel Burroughs

University of Warwick

Single particle tracking (SPT) data is fundamentally stochastic, which makes the extraction of robust biological conclusions difficult. This is especially the case when trying to detect heterogeneous movements of proteins in the plasma membrane, such as changes in diffusivity caused by attachment to the cytoskeleton or receptor clustering. There are currently few methods for detecting this heterogeneity. The main technique for interpreting SPT data remains mean square displacement analysis, which cannot detect changes in motion within a trajectory. We use a hidden Markov model where a (2D) diffusing particle switches between two states with different diffusion coefficients, and subject to Gaussian measurement noise. Working in a Bayesian framework we developed a Markov chain Monte Carlo algorithm to infer the model parameters and hidden state from single trajectories and calculate model selection statistics, such as Bayes factors, to determine if the trajectory supports a 2-diffusion model as opposed to a single diffusion. These methods were applied to a SPT dataset on the LFA-1 receptor molecule on the surface of T cells. We detected the presence of multiple diffusive states, and observed switching between states in a number of trajectories.

Understanding drug behaviour and signalling molecules interactions through the use of a modified EM algorithm for a sparse structure

Zoulikha Zaidi, Ben Forbes, Ton Coolen, Clive Page
Kings College London

We aim to use an approach that allows understanding signalling pathways initiated by the administration of a drug; a bronchodilator. At molecular level, once drugs are administered, a cascade of multi-directional signalling pathways is initiated inside the cell; resulting in airways relaxation. Because of the uncertainty over the interactions between signalling molecules/proteins, the inability to measure most molecules concentrations, and the presence of error in experimental data, it is very hard to build a detailed mathematical model that describes these processes. Therefore, we build a Bayesian network; where the nodes are the signalling molecules/proteins and the edges are the potential interactions between these molecules; believed to have a sparse structure. The parameters that represent molecules interactions, initial concentrations and concentrations of signalling molecules/proteins are considered as random variables. We assume that the system state propagates between two consecutive measurements according to a probability density and its posterior is updated when new measurements are available; using Bayesian formula. We therefore, make use of a modified EM approach that incorporates a sparse prior for the set of parameters. Our goal is to estimate the parameters/interactions that maximise the likelihood of the observation (cell relaxation); confirming/denying potential molecular interactions and pharmacological findings.

New Tools for Model Selection in Gene Regulatory Networks

Catherine Higham, Dirk Husmeier
University of Glasgow

Model selection for kinetic gene regulatory network models is highly challenging due to the number of biological species and nonlinear interactions. In addition, statistical inference methods that require the numerical integration of the data model are computationally expensive. Using state-of-the-art adaptive gradient methods which model the data with Gaussian processes, we address these issues through a number of novel steps. First, we add prior knowledge about the behaviour of the biological species in the form of a periodic kernel. Second, we substantially reduce the complexity of the network by introducing time delays to simplify the modelling of the intermediate protein dynamics. Third, we exploit the fact that, when considering gradients, the interacting biological species can be decoupled into submodels which contain fewer parameters and are individually quicker to run. A Metropolis-Hastings scheme is devised and used to draw samples from the posterior in a Bayesian framework. Using a recent delay differential equation model describing circadian regulation affecting physiology in the mouse liver, we investigate the extent to which deviance information criterion, in conjunction with the sampling scheme, can distinguish between under specified, correct and over specified models.

Reverse engineering chromosome oscillations

Nigel Burroughs, Andrew McAinsh, Jon Armond
University of Warwick

Chromosome movement is powered by kinetochores which form attachments to dynamic microtubules that result in a series of quasi-periodic oscillations during cell division. Directional movements occur because one sister (leading) is attached to shrinking microtubules whilst the other to growing microtubules (trailing). However, it is poorly understood how sisters communicate with each other and how this leads to coordinated changes of direction. To address this we developed a novel reverse engineering (MCMC) Bayesian framework that infers the various mechanical parameters driving oscillatory behavior directly from experimental trajectory data. By fitting a mechanistic model to thousands of sister kinetochore trajectories obtained from 3D super-resolution imaging we characterise for the first time at high resolution kinetochore directional switching and the various forces governing kinetochore movements. We demonstrate that there is a lead sister bias to initiating switching, while the centromeric spring connecting the sisters encodes a switching signature indicative of a causal mechanism - specifically our data suggests a regulation process where the spring tension stabilises the polymerisation state of the trailing sister, preventing its switching, whilst a clock regulates the switching of the lead kinetochore.

Spatio-Temporal Model for Multiple Chip-SEQ Experiments

Saverio Ranciati, Cinzia Viroli, Ernst Wit
University of Bologna and University of Groningen

The increasing availability of ChIP-seq data demands for advanced statistical tools to analyze the results of such experiments. The inherent features of highthroughput sequencing output call for a modeling framework that can account for the spatial dependency between neighboring regions of the genome and the temporal dimension that arises from observing the protein binding process at progressing time points; also, multiple biological/technical replicates of the experiment are usually produced and methods to jointly account for them are needed. Furthermore, the antibodies used in the experiment lead to potentially different IP efficiencies, which can affect the capability of distinguishing between the true signal in the data and the background noise. The statistical procedure proposed consist of a discrete mixture model with an underlying latent Markov Random Field: the novelty of the model is to allow both spatial and temporal dependency to play a role in determining the latent state of genomic regions involved in the protein binding process, while combining all the information of the replicates available instead of treating them separately. It is also possible to take into account the different antibodies used, in order to obtain better insights of the process and exploit all the biological information available.

Model selection for dynamic regulatory networks under l1 penalty and structural constraints

Veronica Vinciotti, Nigel Saunders, Luigi Augugliaro, Antonino Abbruzzo, Ernst Wit
Brunel University London, University of Palermo, University of Groningen

Factorial graphical models have recently been proposed for inferring dynamic regulatory networks from high-throughput data. In the search of true regulatory relationships amongst the vast space of possible networks, these models allow to impose certain restrictions on the dynamic nature of these relationships, such as that Markov dependencies are of low order, i.e. some entries of the precision matrix are a priori zeros, or that the strength of the dependencies depend only on time lags, i.e. some entries of the precision matrix are assumed to be equal. The precision matrix is then estimated by l1 penalised likelihood, imposing a further constraint on the absolute value of its entries, which results in sparse networks. The problem of selecting the optimal sparsity level is traditionally framed in terms of the Kulback-Leibler (KL) divergence. In this paper, we present a KL-motivated model selection criterion for factorial graphical models, by taking into account the a priori structural constraints. We test the performance of this method on simulated data and compare it with existing approaches. Finally, we present an application on a detailed time-course microarray data from the Neisseria meningitidis bacterium, a causative agent of life-threatening infections such as meningitis.

Towards empirical assessment of causal inference [$\star$]

Dr. Sach Mukherjee
Programme Leader at the MRC Biostatistics Unit, University of Cambridge

Sophisticated computational and statistical methods are routinely used to make inferences about the edge structure of molecular networks. Molecular networks are often intended to encode causal relationships between variables and then the object of inference is in effect a causal graph. It is well known from the causal inference literature that strong - and possibly untestable - assumptions are needed to justify causal inference from first principles. Furthermore, causal inference can easily be led astray by factors such as unobserved confounders and certain additional factors specific to systems biology may exacerbate these concerns. How then can we tell whether network learning methods are really effective in a given setting? I will discuss our recent efforts to develop empirical approaches by which to assess causal network learning using experimental data. These approaches were used in the 2013 DREAM network inference challenge and I will use data and results from the challenge to illustrate the key ideas.

Data-driven inference of causal molecular networks and systematic assessment of inference performance

Steven Hill, Sach Mukherjee, Nicole K. Nesser, Paul T. Spellman
MRC Biostatistics Unit, Oregon Health and Science University

Causal interplay between molecular components is central to regulation of cellular behaviour, and it is increasingly clear that molecular networks may depend on biological context, such as cell type or disease state. Therefore, in conjunction with appropriate experimental designs, there is a need for robust and scalable statistical approaches for inference of context-specific, causal networks. In this work we focus on protein signalling networks in breast cancer and utilise directed graphical models known as dynamic Bayesian networks (DBNs) to infer networks from time course proteomics data with interventions on network nodes. Our approach models the intervention conditions in the data, allows for integration of existing biology within a Bayesian framework, and exploits a connection between variable selection and network inference to enable exact, yet efficient, calculation of posterior probabilities of interest. Due to the challenging nature of causal network inference, it is necessary to empirically assess the ability of methods to recover causal relationships. Methods are often assessed using simulated data, where a gold-standard causal network structure is available. However, for real-world systems such as that under study here, there is no gold-standard available. We propose an approach that leverages the interventional data to perform systematic assessment of inferred causal networks and use this approach to empirically test our analyses. Furthermore, we see evidence that signalling network structure does indeed depend on biological context. These data and assessment approaches were also used in the 2013 DREAM network inference challenge. The 70 final submissions to the challenge allowed for a comprehensive, unbiased assessment of many causal network inference methods, applied in a mammalian setting. Time permitting, I will discuss the challenge itself and present key results and insights from our post-challenge analyses.

Estimation and control of cell populations [$\star$]

Prof. John Lygeros
Head of the Automatic Control Laboratory, ETH Zurich

Feedback mechanisms are at the heart of many cell functions, including genetic regulation. Engineering such mechanisms in living cells synthetically has proved to be a challenging task, however. This is partly due to the difficulties associated with making the process robust against cell-to-cell variability. We discuss how stochastic analysis and control methods can be used to shed light into the uncertainty affecting these systems. We first investigate how modeling and analysis methods can be extended to account for stochasticity not only at the level of individual cells, but also at the level of cell to cell variability. We then use the resulting models for system identification, optimal experiment design for strain characterization, and ultimately regulation of gene expression. We demonstrate the methodological contributions by experimental results on a yeast strain, using a light-sensitive transcription factor as the input and flow cytometry measurements of the resulting fluorescent protein as the output.

Modelling transcriptional regulation of circadian genes of the Arabidopsis Thaliana

Silvia Calderazzo, Bärbel Finkenstädt
University of Warwick

A setting where two Transcription Factors (TF) are regulating the mRNA production of a putative child gene is assumed in this work. This is motivated by the availability of an experimental data-set studying the regulation of a subset of circadian genes of the Arabidopsis Thaliana by LHY Protein. In order to explain the wide range of observed phases in the regulated genes, a second unobserved Transcription Factor is assumed. A stochastic model describing the exact behaviour of the system, and the mechanisms of activation and repression through the binding and unbinding of Transcription Factors to the promoter, is first developed. However, model reduction is required for inferential purposes. Under specific assumptions regarding the system size and the time-scale of the reactions involved, approximation to the original model are available. The transition densities of the reduced underlying stochastic process are approximated according to the Extended Kalman-Bucy Filter, and the likelihood takes into account the presence of destructive sampling in the experimental design. The final model also incorporates the reconstruction of the unobserved TF. Parameter inference is carried out in a Bayesian framework with an MCMC algorithm, where bimodality arising in the posterior density is addressed with tempering techniques.

Robust Reconstruction of Causal Graphical Models from Genomic Data

Séverine Affeldt
Hervé Isambert, Institut Curie

The reconstruction of causal graphical models through efficient constraint-based approaches is consistent if a correct list of conditional independences is available. Yet, in practice, these independences, ascertained from finite observational datasets using statistical significance levels, are not robust to sampling noise. We proposed a more robust approach to discover structural independences based on the ranking of their most likely contributing nodes. Our algorithm, 3off2, iteratively takes off the most likely conditional-3-point information from the 2-point information between each pair of nodes to progressively derive the conditional independences. This inference approach was used to reconstruct somatic alteration pathways that drive tumor progression. While advances in massively parallel sequencing technologies are providing biologists with larger cross-sectional datasets, identifying the genes involved in the causal multistep process of the tumorigenesis still remains a difficult task, in particular due to the mutational signature diversity across cancer (sub)types. However, 3off2 takes advantage of the heterogeneity between tumor samples to learn the most likely temporal sequences of somatic alterations during malignant transformation. The robust causal inference of the distinct genetic alteration pathways could empower researchers to envision new diagnostic tests and innovative therapeutic drug targets.

A comparison of approximation methods for stochastic biochemical networks [⋆]

Dr. Ramon Grima
Reader in Stochastic Systems Biology, University of Edinburgh

Exact solutions of the chemical master equation are only known for a handful of simple biochemical systems. Various approximations have thus been devised to circumvent this problem. In this talk, I will present an overview of our work over the past few years which clarifies the accuracy and the relationship to one another, of three common approximations (the linear-noise approximation, the chemical Fokker-Planck equation and moment-closure approximations) for systems whose dynamics are influenced by intrinsic noise. I will also present novel approximation methods based on the system-size expansion which overcome some of the deficiencies of the aforementioned three approximations. Finally I will discuss recent work on determining the accuracy of a popular approximation method for systems influenced by both extrinsic and intrinsic noise and show how one can construct a fast and efficient, exact simulation algorithm for such systems.

Incorporating contemporaneous relationships among gene expression time series into the model selection of gene networks

Osvaldo Anacleto
Roslin Institute, University of Edinburgh

Dynamic Bayesian networks (DBNs) have been extensively applied in gene network modelling, with a variety of methods available to estimate graphical structure. These models usually assume that parents of a time series at a given time t take values at previous time periods. However, gene expression relationships can occur on different time scales: relationships occurring on a minute-by-minute level are unlikely to be captured by current DBNs when using hourly gene expression data, for example. In this context, dynamic graphical models which allow contemporaneous relationships among its nodes can provide better estimates of gene network structures. The linear multiregression dynamic model (LMDM) is a DBN which not only allows contemporaneous relationships in its graph, but also enables closed-form updating of its parameters. It will be shown in this talk how the LMDM can estimate gene networks by using integer programming, resulting in more accurate results compared to some current methods when analysing benchmark gene expression datasets. This talk will also discuss the application of integer programming to learning dynamic chain graphs, which can accommodate gene expression relationships not usually considered in gene network modelling

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Joint Estimation of Multiple Related Biological Networks

Chris Oates, Jim Korkola, Joe Gray, Sach Mukherjee
University of Warwick, Oregon Health and Science University, University of Cambridge

In many applications, data are collected from multiple related but non-identical biological samples whose underlying biological networks may differ but are likely to share features. Here we present a hierarchical Bayesian formulation for joint estimation of multiple networks in this non-identically distributed setting. The statistical approach is general: given a suitable class of graphical models, it uses an exchangeability assumption on networks to provide a corresponding joint formulation. Motivated by emerging experimental designs in high-throughput proteomics, we focus on time-course data with interventions, using dynamic Bayesian networks as the graphical models. We introduce a computationally efficient, deterministic algorithm for exact joint inference in this setting. We provide an upper bound on the gains that joint estimation offers relative to separate estimation for each network and empirical results that support and extend the theory, including an extensive application to proteomic data from human breast cancer cell lines.

Stochastic Modelling of Genetic Interaction in Budding Yeast [$\star$]

Prof. Darren Wilkinson
School of Mathematics and Statistics, Newcastle University

Saccharomyces cerevisiae (often known as budding yeast, or brewers yeast) is a single-celled micro-organism that is easy to grow and genetically manipulate. As it has a cellular organisation that has much in common with the cells of humans, it is often used as a model organism for studying genetics. High-throughput robotic genetic technologies can be used to study the fitness of many thousands of genetic mutant strains of yeast, and the resulting data can be used to identify novel genetic interactions relevant to a target area of biology. The processed data consists of tens of thousands of growth curves with a complex hierarchical structure requiring sophisticated statistical modelling of genetic independence, genetic interaction (epistasis), and variation at multiple levels of the hierarchy. Starting from simple stochastic differential equation (SDE) modelling of individual growth curves, a Bayesian hierarchical model can be built with variable selection indicators for inferring genetic interaction. The methods will be applied to data from experiments designed to highlight genetic interactions relevant to telomere biology.

Likelihood free inference for Markov processes: a comparison

Jamie Owen, Darren Wilkinson, Colin Gillespie
Newcastle University

Approaches to Bayesian inference for problems with intractable likelihoods have become increasingly important in recent years. Approximate Bayesian computation (ABC) and "likelihood free" Markov chain Monte Carlo techniques are popular methods for tackling inference in these scenarios but such techniques are computationally expensive. In this paper we compare the two approaches to inference, with a particular focus on parameter inference for stochastic kinetic models, widely used in systems biology. Discrete time transition kernels for models of this type are intractable for all but the most trivial systems yet forward simulation is usually straightforward. We discuss the relative merits and drawbacks of each approach whilst considering the computational cost implications and efficiency of these techniques. In order to explore the properties of each approach we examine a range of observation regimes using two example models. We use a Lotka-Volterra predator prey model to explore the impact of full or partial species observations using various time course observations under the assumption of known and unknown measurement error. Further investigation into the impact of observation error is then made using a Schlogl system, a test case which exhibits bi-modal state stability in some regions of parameter space.

Bayesian inference for Markov jump processes with informative observations

Andrew Golightly, Darren Wilkinson
Newcastle University

In this paper we consider the problem of parameter inference for Markov jump process (MJP) representations of stochastic kinetic models. Since transition probabilities are intractable for most processes of interest yet forward simulation is straightforward, Bayesian inference typically proceeds through computationally intensive methods such as (particle) MCMC. Such methods ostensibly require the ability to simulate trajectories from the conditioned jump process. When observations are highly informative, use of the forward simulator is likely to be inefficient and may even preclude an exact (simulation based) analysis. We therefore propose three methods for improving the efficiency of simulating conditioned jump processes. A conditioned hazard is derived based on an approximation to the jump process, and used to generate end-point conditioned trajectories for use inside an importance sampling algorithm. We also adapt a recently proposed sequential Monte Carlo scheme to our problem. Essentially, trajectories are re-weighted at a set of intermediate time points, with more weight assigned to trajectories that are consistent with the next observation. We consider two implementations of this approach, based on two continuous approximations of the MJP. We compare these constructs for a simple tractable jump process before using them to perform inference for a Lotka-Volterra system. The best performing construct is used to infer the parameters governing a simple model of motility regulation in Bacillus subtilis.

Diagnostics for assessing the accuracy of approximate stochastic simulators

Colin Gillespie
Newcastle University

Solving the chemical master equation exactly is typically not possible. Instead, we must rely on simulation based methods. Unfortunately, exact simulation results in simulating every reaction that occurs which may preclude the use of exact simulators for models of any realistic size. Approximate simulation techniques therefore become important. We describe a general framework to assess approximate stochastic simulators. By constructing an efficient space filling design over the parameter region of interest, we present a number of useful diagnostic tools. In particular, we leverage the normality assumption of the linear noise and moment closure approximations.

5 Poster Abstracts

Modeling Transcription regulation through the Network Switch Model

Giorgos Minas, Dafyd Jenkins
University of Warwick

We develop novel methodology for modelling transcription regulation of target genes through a set of potential transcription factors. The target mRNA expression profiles are fitted by a piecewise linear ODE model where the transcription τ-rate 'switches' at specific time points due to changes in the activity of its regulators. That is, transcriptional switches occur at times where a regulator's expression surpass (or falls below) a threshold level to become activated (or deactivated). Multiple experiments can be fitted simultaneously while constraints on τ rates ensure within- and between-experiment consistency of our results. Bayesian methodology is employed to provide a posteriori answers on key biological questions, namely: how many and which are the factors for regulating mRNA transcription of a target gene, but also to provide a description for the nature of the derived regulatory associations. A simple RJ MCMC is used to implement our methods allowing for trans-dimensional jumps across models with different number of regulators. We apply our methods to data from PRESTA (Plant Responses to Environmental Stresses in Arabidopsis) to derive networks of genes maintained across multiple conditions. Interesting results are obtained including factors which appear to turn activators to deactivators and vice versa.

Comparing the Topologies of Urine-Peptide Based Diseasomes and Protein-Protein Interaction Networks

Joan Planas-Iglesias, Judith Klein-Seetharaman
University of Warwick

The diseasome is a network in which nodes are gene-products and edges connect such products if they are involved in the same disease. Here, we used mass-spectrometry data from urinary polypeptides of over 13000 patients involved in 46 different clinical conditions (Proteomics Clin Appl. 2011 5:367-74) to obtain protein-disease correlations. The urine peptide spectra of samples from patients suffering from the same condition are highly correlated and have been used in disease diagnosis. Here, we transform the urine peptide data into a diseasome by calculating correlation coefficients for mass spectra-disease pairs and using a hard threshold to define edges. While typically in this process a significant correlation threshold is set assuming a scale-free topology for the resulting network, also known as soft threshold, the use of non-topological criteria to define relevant correlations (hard threshold) has the advantage that topological comparisons between the resulting diseasome and other biological networks can be made. We have investigated the topological robustness of the urine peptide based diseasome network in comparison to the respective protein-protein interaction network. We anticipate that analysis of the results will allow gaining insight into the underlying mechanisms for known co-morbidities or perhaps discover new ones from the network topology.

Hierarchical Bayesian stochastic analysis of oscillatory multiple single cell Nrf2 protein levels

Simone Tiberi, Bärbel Finkenstädt
University of Warwick

Our work focuses on the hierarchical analysis of multiple single cell Nrf2 reporter levels in nucleus and cytoplasm. Nrf2 is a transcription factor that regulates the expression of several defensive genes protecting against various cellular stresses. Our analysis aims to gain an insight into this essential cellular protective mechanism. We propose a reaction network based on five reactions, which include a distributed delay and a non-linear term, for the amount of Nrf2 in nucleus and cytoplasm. The diffusion approximation is used, jointly with the Euler-Maruyama approximation, to obtain an approximated likelihood of the process. We also employ a data augmentation method: a bridging procedure. Furthermore, to make use of multiple single cell data, we embed the model in a hierarchical framework. A measurement equation, which involves a proportionality constant and a normally distributed white noise, is necessary to relate the original unobserved population levels, X, to the observed ones, Y. A Bayesian analysis is performed alternatively sampling the parameters of the model, given the reconstructed process X, and the unobserved process X. conditional on the parameters and the observed values Y. We will show simulation studies' results proving the validity of the methodology, which will then be applied to real data.

Updated mathematical model and fed-batch strategies for Polybetahydroxybutyrate (PHB) production by Alcaligenes Eutrophus

Arjun Atreya, Ashok K. Srivastava
Netaji Subhas Institute of Technology

Growth and PHB storage kinetics of A. Eutrophus were studied in a batch cultivation process. Effect of initial N/C ratio on maximum specific growth rate was observed in range 0.03-0.4. Maximum growth rate was observed at N/C ratio 0.9. Structured mathematical model was proposed. Model parameters were evaluated using the actual batch fermentation data. The model was used to simulate nutrient feeding profiles for enhanced PHB production in a fed batch fermentation.

Multivariate models to predict progression of renal disease

Ana Cristina Bico Matos, Carla Henriques, Bernardo Faria, Manuel Pestana
Polytechnic Institute of Viseu, University of Porto

Immunoglobulin A nephropathy (IgAN) is a kidney disease with a wide spectrum of presentation, progress and also of therapeutic approaches. Research on means of prediction of pathogenesis and progression of IgAN disease is, of course, of great clinical interest. Recent studies have highlighted the association of some molecules with pathogenesis and progression. This study involves four of these molecules, C4d (complement lectin pathway involvement), CD3 (T-cell marker, traducing interstitial inflammation), Transglutaminase 2 (TGase-2, involved in tissue fibrosis development), and p-ERK 1/2 (protein kinase intracellular signaling molecule) in order to obtain a panel of immunohistological biomarkers, and assess its predictive value for the disease course. We studied 74 renal biopsies from patients with IgA nephropathy, with a follow-up of 48 months (in average), of which 20 present progressive kidney disease and 54 non progressive kidney disease. Resorting to univariate statistical analysis and multivariate models, logistic and Cox regression models, we show that the combination of two histological biomarkers (C4d and CD3) can be a powerful predictor of IgAN progression and a potential useful tool for the clinical approach of this disease.

Identifying Spatially Correlated Changes in methylation Profiles Using Kernel Methods

Tom Mayo, Gabriele Schweikert, Guido Sanguinetti
University of Edinburgh

DNA methylation is an intensely studied epigenetic mark associated with many fundamental biological processes of direct clinical relevance. Bisulfite treatment of DNA followed by next generation sequencing provides quantitative methylation data at base pair resolution. However, statistical modelling of such data is challenging. Current approaches do not consider higher order features of the data, so that spatially correlated changes are ignored. A recent paper has shown that the shape of the methylation profile change is predictive of gene expression. Furthermore, parametric tests require high coverage and replication and are prone to overconfidence under high coverage conditions. We introduce a non-parametric test, M3D, based on the maximum mean discrepancy to address such issues. M3D uses kernel methods to capture spatially correlated changes in methylation profiles and displays improved power over existing methods in challenging conditions. The method is freely available via Bioconductor as package M3D.

Delegate Joining Instructions
Warwick Conferences' Conference Park

We are delighted that you will be joining us at the University of Warwick. We hope that the information provided in this document will help you get the most from your event. Please bring these instructions with you as you will find them useful whilst you are on campus.

The Conference Park is on the main campus of the University of Warwick located on the outskirts of Coventry, which is accessible by road, rail and air. You can download further information from the website at www.warwickconferences.com, following the link 'how to find us'. A further link can be found for any relevant traffic information
http://www.warwickconferences.com/delegates/delegates-conference-park

The Conference Park is the name given to the facilities provided by Warwick Conferences on the main University campus.

Getting here:

University and local roadworks 2014

- The University in conjunction with the local areas are working on a major development to improve the roads in and around the University.
- Specifically aiming to improve the safety and capacity of our roads and the appearance and accessibility of major areas of campus.
- This all starts this summer with major changes to Gibbet Hill Road, starting on 23 June 2014 and due to end in October 2014, with sections of the road closed at times.
- We recommend that you allow approximately an additional 30 minutes for your journey (and more at standard rush hour times) as there may well be congestion around campus. On approach to campus, please be aware of diversion signage and follow as directed.
- Once you're on campus, please pay close attention to signage – diversions and traffic management will change on a daily basis depending on what work is being carried out - staff will be located at car parks and other key areas to assist and advise.

Which direction to approach from:

- For the Conference Park please head for Westwood Heath/Kirby Corner Road. If your journey currently brings you along the A46 then you will need to carry along onto the A45 (there will be diversion signs to the A45).

Where to park:

If you're arriving at Central Campus including:

- Conference Park Reception
- Rootes Building
- Warwick Arts Centre
- Ramphal Building

Please use car parks 7, 8, 8a and 15

Car parking:

Once you arrive on campus please look out for the blue Warwick Conferences signage to direct you to the car parks and conference venues.
Complimentary car parking is available for conference delegates in the allocated car parks on campus (7, 8, 8a and 15). On entering the car park, you will be provided with a pass for these car parks and this should be placed in the window of your vehicle, if arriving after 19.00hrs and some weekends it may be necessary for you to collect a pass from the Conference Reception in the Student Union Building.
Disabled parking spaces are available close to the entrance of main buildings.

As a University campus, from time to time these car parks become full and when this happens alternative parking will be available, which you will be directed to. We advise that you allow sufficient time, for up to a ten minute walk to get to your destination on the Conference Park from the car parks. Some of the car parks are not adjacent to the registration and accommodation areas, it is therefore advisable once you have parked, for you to take your luggage to Conference Reception where you will be able to leave it with the team in the left luggage facility.
Your Event Organiser can provide further information regarding car parking arrangements.

Accommodation:

Please check with your Event Organiser as to which type of accommodation has been reserved for your event and what facilities are available.

Conference Reception:

Located within the Students Union Building. The Reception team are available to answer your queries between 07:00 – 23:00. Here you can also:

- Find out general information
- Arrange for secure luggage storage
- Validate your car parking token
- Collect information on how to connect to the wifi around campus
- Ask about any lost property
- Request additional bedroom supplies such as pillows, blankets, clock radio, bath mat or a bedside lamp

Keys:

You will be provided with one key or key card which will access your room and entry door to the residence. Keys can be left at Conference Reception, Rootes Restaurant (in Rootes Building) or one of the boxes situated in the entrance halls of each residence on the day of your departure.

Bedroom check in/out:

Bedroom keys will be available from 15:00 to 23:00 at Conference Reception. If you plan to arrive after 22.45, please contact Conference Reception to arrange late key collection (wcpreception@warwick.ac.uk). Rooms need to be vacated by 09:30 on your day of departure and all luggage and belongings to be removed at that time. Please inform Conference Reception on arrival, of any difficulties you may have in the unlikely event of an evacuation from your accommodation (e.g. hearing or mobility difficulties).

Disability services:

The University of Warwick aims to be accessible and welcoming to everyone and we are committed to making your visit as easy and enjoyable as possible. If you have any particular requirements that we should be aware of, hen please discuss these with your Event Organiser.

Internet access across campus:

If you would like to access the wifi network then please ask at Conference Reception or any of the Information Points around campus (e.g. Rootes Building and Warwick Arts Centre) for details. Alternatively log onto your device and go to your web / wireless browser:

1. Connect your device to the **'Warwick Guest'** wireless network.
2. Upon your first attempt to access online content with the web browser, you will be redirected to the Warwick Guest Wireless web page (most Apple devices will automatically perform this step).
3. If you already have a valid Warwick Guest account, please login with those credentials, otherwise please continue to create yourself a Warwick Guest account. N.B. This is **NOT** the same account used on the 'conferences' wireless network.
4. Click the link within the sentence 'Click here to create an account' and select 'Attending a conference'.
5. Please provide your details, including a valid mobile phone number, to which you generated guest login will be sent.
6. Follow the web links to return to the Warwick Guest Wireless webpage and login.
7. If you do not have a mobile phone, choose the option 'Click here to register if you do not have a mobile phone' at the bottom of the page to have your login details sent to your email address.

Food and Drink:

All meals are provided in Rootes Restaurant located on the first floor of Rootes Building for all delegates (unless your programme indicates otherwise). The restaurant offers an assisted style service of breakfast, lunch and dinner including a range of hot and cold drinks. Your Event Organiser will be able to advise you regarding the specific arrangements for your event. Please have with you your conference badge or room key to gain access to the restaurant. If you have any special dietary requirements then please inform your Event Organiser.

The bar is located on the first floor of Rootes Building and is the ideal place to network and relax after a day's session. There are also alternative bars in Warwick Arts Centre and Students Union building (check opening times locally)
Payment for all sundry items is by cash or credit card payment only.

Shops, Banks, Cafés and Bars on campus:

The campus has many facilities available to all delegates, for all information and opening times please see the website: http://www.warwickretail.com . Warwick Arts Centre cinema offer discounted cinema tickets at £5.50, these can be purchased from the box office and proof of delegate status is required (not applicable for Met Opera Live or NT Live screening).

Sports facilities:

Delegates have use of some of the comprehensive sports facilities including swimming and fitness suite free of charge. Other facilities are available for a nominal charge which will need to be booked in advance. Details and opening times are available at Reception or by visiting the website below. Delegates need to present their bedroom key at the reception to gain access. See www2.warwick.ac.uk/services/sport for more information.

For more information:

You can also refer to our Frequently Asked Questions document (FAQ's) which can be obtained from your Event Organiser or our website: http://www.warwickconferences.com/delegates/delegates-conference-park

Frequently Asked Questions
Warwick Conferences' Conference Park

Location and travel

Where in Coventry is the University of Warwick?
Just four miles from Coventry City centre, we are sited at the hub of the central motorway network.

What is the Conference Park?
This is the name given to the facilities provided by Warwick Conferences on the main University campus. The building used for dining and bars is Rootes Building and Conferences Reception is within the Students Union Building.
A link can be found for all relevant traffic information at: http://www.warwickconferences.com/delegates/delegates-conference-park

Once you arrive on campus please look out for the blue Warwick Conferences signage to direct you to the car parks and conference venues.

Where is the nearest Mainline Rail Station?
Coventry Intercity station is only four miles from the University. A taxi would cost approximately £11.00 from Coventry station to the University campus. Birmingham International Railway Station is also close to campus and a taxi from this location would cost approximately £27.00.

Is there a taxi rank on campus?
Taxis are available on Health Centre Road opposite Warwick Arts Centre at most times of the day. Alternatively you can contact Conference Reception for more information and relevant phone numbers.

Can I travel by bus from Coventry Railway Station or Bus Station?
The Number 12 bus runs from Coventry Bus Station via Coventry Train Station to the University

Is car parking free or do you have to pay?
The Conference Park offers limited complimentary parking in specified car parks. You will need to validate your parking token at Conference Reception. Your Event Organiser will be able to advise you further.

If I have a minibus or high sided vehicle – where can these be parked?
Minibuses and high sided vehicles can park on the ground floor (outside section) of Car Park 15. It would be advisable to let your Event Organiser know of your requirement for specific car parking, as most of the University car parks are multi storey.

Accommodation

What time can I collect my bedroom key?
Check in for the Conference Park is from 15:00 onwards. Keys are collected from Conference Reception, unless you have been notified of a different location by your Event Organiser.

What will happen if I arrive after 22.45 and Conference Reception is closed?
Conference Reception is open until 23:00. If you are planning to arrive later than 22.45, please call in advance on 02476 528910 to arrange key collection from an alternative location. Once Reception is closed there is clear signage on the main door explaining the process for late arrivals.

Will we stay in halls of residence?
All Conference Park accommodation is student style either a standard or en-suite room. Your Event Organiser will be able to advise you on which type of accommodation you have been allocated.

Do any of the residences have lifts?
Some residences do. If you have a particular requirement then please discuss with your Event Organiser.

What time do I need to check out of my room?
Check out time is 09:30 and all luggage and belongings should be removed at that time.

What electrical supply is available in the bedrooms?
Electricity is supplied at 220/240v and 50 cycles AC. Most foreign appliances will require an adaptor or transformer. Adaptors are available to buy at Costcutter supermarket.

Are there any laundry facilities on campus?
The launderette is situated between Rootes Building and Rootes residences, opening times are available from Conference Reception for self-service washing and drying. There are also laundry facilities available in some of the residences. All machines require the correct change and you will need to provide your own washing powder and fabric softener.

Will I have access to a kitchen within my accommodation block?
Each delegate will have access to a kitchen although this may not be directly adjacent to their bedrooms. Please note these areas will not contain any cooking equipment or utensils.

Facilities on campus

What Leisure facilities are there and do delegates have access?
Delegates may use some of the University's Leisure facilities free of charge providing they take along their bedroom key or delegate name badge as a means of identification. Other facilities are available for a nominal charge and may need to be booked in advance. The towel from your bedroom can be taken to the Sports Centre, alternatively you can hire an additional towel at the Sports Centre for £1.75. Please see http://www2.warwick.ac.uk/services/sportscentre for further details.

What religious services are available on campus?
The Chaplaincy is a vibrant space for all members of the University community and visitors. To gain access to the Chaplaincy, please ask at Conference Reception for details.

Are there any cash machines or banks on campus?
There are branches of Barclays and Santander, both have cash machines in the Students Union Building (directly next to Rootes Building).

Where can I access my emails?
Conference Park delegates can access the wifi network around campus and within their accommodation block, please ask at Conference Reception or any member of the team for the details of how to connect. A limited number of computers are available for delegate use in the Conference Reception.

If I am having mobility problems is there anything you can do to help?
Mobility scooters are available for conference delegates; please ask at Reception for more information.

What should I do if I am not feeling well?
Please contact Conference Reception on 02476 522280, who will ensure a message is given to your Event Organiser. We do not have a resident doctor available for conference delegates, but in the event you require medical attention, this can be done via our 24 hour Security Team on 02476 522083. Alternatively there is a Walk In Medical Centre in Coventry - click here for more details.

Is there anywhere on campus I can buy toiletries or get pharmacist advice?
There is a pharmacy located in the Students Union Building and Costcutter supermarket also sells a variety of items. These buildings are located next to Rootes Building.

Food and drink on campus

I have a particular special dietary need – can you manage this?
The Conference Park Team can manage all special dietary needs if they are aware of the requirement in advance. Please ensure you communicate this to your Event Organiser before arriving at Warwick. Once on campus, please ask any of the team in the restaurant for more information or guidance.

Where can I purchase alcohol on campus?
There are three licensed buildings where you can purchase alcohol for consumption within or outside of that building. These are:

- Rootes Building
- Warwick Arts Centre
- Students Union Building
- Costcutter is also a licensed retail shop, however alcohol purchased from Costcutter cannot be consumed in any of the above licensed areas.

Local Area

What is there to do in the local area?
There is a wide range of social and sports facilities available on campus, including woodland walks, a sports hall, swimming pool and squash courts. The largest Arts Centre outside of London - Warwick Arts Centre is also onsite where you can watch the latest cinema releases and/or performances. Coventry city centre is only three miles away and the towns of Warwick, Stratford Upon Avon and Leamington are close by.

Where are the nearest shops to campus?
There are a number of retail shops on campus including Costcutter supermarket, Pharmacy, Bookshop and Hairdressers, for any other requirements there is:

- Cannon Park Shopping Centre is within ten minutes walk and has a large supermarket and several smaller retail shops
- Central Six Retail Park is a ten minute car journey (next to Coventry Railway Station) and has a large chemist and some good sized high street stores

Other useful information

What signage should I look out for on campus?
University Signage – these are positioned around campus highlighting all Academic Buildings and social spaces – they are white rectangular blocks

Warwick Conferences / Conference Park signage – these are blue swing signs used to highlight car parking spaces and spaces used for conferences. Look out for the conference logo.

Are there any other useful items I could bring with me?

- An umbrella – as you will be required to walk between some buildings
- Any sports equipment that you may require during your stay
- Additional towels for use in the Sports Centre
- Suitable clothing and footwear
- Phone charger

Opening times

Summer vacation: Saturday 28 June – Saturday 28 September 2014

Café Library
Monday – Friday 8am – 4pm*
Saturday – Sunday 10am – 4pm
* The extension will be open 8am – 6pm

Café Humanities
Monday – Friday 8.30am – 3pm

Le Gusta
Monday – Friday 12pm – 10pm**
Saturday – Sunday 5pm – 9pm

University House restaurant
Monday – Friday 8am – 2.30pm

University House atrium coffee bar
Monday – Friday 8am – 6pm

Fusion
Monday – Saturday 12pm – 3pm

Costa
Monday – Friday 8am – 5pm
Saturday – Sunday 9am – 4pm

The Bookshop
Monday – Friday 9am – 5.30pm

Warwick Business School
Monday – Friday 8.30am – 3pm

"Belle" on the piazza
Lunch and Evening
(see local advertising and twitter)

Library Coffee Bar
Monday – Friday 8.30am – 4pm

Café Social (closed August)
Monday – Friday 9.00am – 2.00pm

Café Gibbet Hill
Monday – Friday 8am – 4.30pm

Café Bar
Monday – Saturday 8am – 9pm
Sunday 3pm – 8.30pm

Theatre Bar
Dependent upon performances

The Bar (serving bar food)
Monday – Sunday 12 noon – 11pm

Costcutter
Monday – Friday 8am – 8pm
Saturday 9am – 8pm
Sunday 11am – 5pm

Café Westwood
Monday – Friday 8am – 3pm

H-van (behind WMG building)
Monday – Friday 9am – 3pm

** Last food orders 9pm. Please note that in exceptional circumstances management reserve the right to change opening times without prior notice.