Latest Advances in the Theory and Applications of Design and Analysis of Experiments

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Design and analysis of experiments is an area in statistical methodology, which has applications in many research fields where experiments are performed to develop new theory and/or improve the quality of processes and services. For example, experiments are continually carried out to investigate and improve manufacturing processes, understand climate changes, provide better utilization of large-scale primary care services, evaluate environmental damages, and develop more effective drugs for patients, to name a few. Optimal design techniques are also used in education testing, cryptology or fMRI analysis of brain data. Even small improvements in methodology can have huge effects in applications. Because of rapidly rising costs in experimentation, researchers are increasingly interested in using efficient designs that save costs without sacrificing the quality of ensuing statistical inferences. In toxicology, for example, in addition to saving labour, time and material cost, researchers are increasingly under pressure to use the fewest possible animals in laboratory research.

There have been many exciting new developments in this area in the last two decades. In particular, researchers have made advances in both theory and applications of optimal designs for mixed effects models, longitudinal models and nonlinear models, including more efficient designs in health care studies, computer experiments, and experiments for processes with time or space dynamics. The main aims of the workshop were to develop new theory for optimal design for new and more challenging problems, apply novel applications of optimal designs to new problems and keep us up to date of the state-of-the-art optimization techniques used in engineering and computer science. Some focus areas of the workshop are described below.

1 New Theory and Construction Methods for Nonlinear Models

The theory of optimal designs for non-linear models is very important because they have many applications in the medical and pharmaceutical sciences, biometry and in various other industrial experiments. However, most design work has focused on models with independent and normally distributed errors, fixed effects, and assuming the outcome is either continuous or binary. The workshop provided a forum to stimulate development of advanced methods for constructing optimal designs in nonlinear models with mixed effects, longitudinal models, and models with non-normally correlated errors or models with outcomes that may comprise of continuous and discrete responses. Progress was also made in the construction of optimal designs with correlated observations, which has particular mathematical challenges, due to the non-convexity of the optimization problems. Other attendees had already made, and continue to make, important contributions to design in health care and clinical trials. These include strategies for designing studies where the main outcomes are categorized (treatment success, partial success or failure), optimal randomization allocation plans for patients in a multi-arm clinical trial, and optimal design strategies for testing in enzyme-kinetic studies.

Two different approaches of experimental design for the so called Fractional Polynomials (FP) family of models were described, independently, by Professors Steven Gilmour and Jesus López-Fidalgo. This family has been shown to be much more flexible than polynomials for fitting continuous outcomes in the biological and health sciences. In particular, being linear models they can be used instead of a variety of non-linear models that add much complexity to the usual inferences. Despite their increasing popularity, design issues for FP models had never been addressed. D- and I-optimal experimental designs were computed for prediction using FP models. Detailed proofs of the closed-formed design were given when possible. Otherwise numerical computations were made. Their properties were shown and a catalogue of design points useful for FP models was provided in illustrative graphics. As applications, linear mixed effects models for longitudinal studies were considered. An example using gene expression data was considered by Professor López-Fidalgo, comparing the designs used in practice. Taking into account the final choice of one of the potential models, an interesting problem is finding designs for effective model discrimination for FP models. They are exploring KL-optimality and he showed some of their advances.

On the other hand Professor Gilmour noted that with the availability of routines for fitting nonlinear models in statistical packages, FP models are increasingly being used. However as in all experiments the design should be chosen such that the model parameters are estimated as efficiently as possible. The design choice for such models involves the usual difficulties of nonlinear models design. He presented Bayesian optimal exact designs for several fractional factorial models. The optimum designs were compared to various standard designs in response surface problems. Some unusual problems in the choices of prior and optimization method were noted. As an introduction to his presentation Professor López-Fidalgo made some comments about the present and future of experimental design. In particular he mentioned the paper "Manifesto for reproducible science" published recently in Nature, where the authors, coming from different sciences, ask for a rigorous research methodology and give key measures to optimize the scientific process. He pointed out the word 'design' appears 25 times in 7 pages in all sections of the paper.

Experimental design applications for discriminating between models have been hampered by the assumption to know beforehand which model is the true or more adequate one, which is counter to the very aim of the experiment. Previous approaches to alleviate this requirement were either symmetrizations of asymmetric techniques such as compound T-optimality, or Bayesian, minimax and sequential approaches. In their joint talk Professors Radoslav Harman and Werner Müller presented a novel, genuinely symmetric criterion based on a linearised distance between mean-value surfaces and the newly introduced notion of nominal confidence sets . The computational efficiency of the proposed approach was shown and a Monte-Carlo evaluation of its discrimination performance on the basis of the likelihood-ratio was provided. Additionally these authors demonstrated the applicability of the new method for a pair of competing models in enzyme kinetics.

Professor Anatoly Zhigljavsky (Dette et al. 2016, 2017) reviewed a series of works related to optimal designs with correlated errors and noted the potential importance of implementing designs with correlated errors in practical applications. His talk highlighted new and important theoretical investigations toward that direction. He presented a complete solution of this challenging optimal design problem for a broad class of regression models and covariance kernels. As a by-product he derived explicit expressions for the BLUE in the continuous time model and analytic expressions for the optimal designs in a wide class of regression models. Professor Anatoly Zhigljavsky also reviewed the celebrated Sacks-Ylvisaker approach and discussed several approximate methods of construction of optimal estimators.

Yu Shi from UCLA Biostatistics Department described her group's recent research into utilizing advanced optimization and integration techniques to find Bayesian optimal designs for random effects models, which potentially has profound applications in HIV studies, PK/PD studies and many other studies in biomedicine. She also talked about using these techniques in developing biomarkers in oncology studies. This work is interesting both methodologically and in practice, and the group puts great efforts into developing user-friendly software that is promising to benefit scientist and practitioners at large. Her message reinforced Dr. Kim's use of novel algorithms used by engineers and computer scientists to solve hard design problems. This algorithm is a member of the class of nature-inspired metaheuristic algorithms which has been shown to be very flexible, assumptions free and easy to implement and use. They are powerful in that they have been reported in computer science and engineering arenas to be able to solve optimization problems with hundreds of variables in a relatively very short period of time. In short, they offer exciting opportunities and great promise when current numerical methods in statistics do not work well. When designing a study for a complicated nonlinear problem or a high dimensional design problem, these algorithms can also help determine the structure of the optimal design quickly and hence help the researcher makes an informed guess on the correct number of points required, their locations and the number of replicates at each of the design points. Subsequent applications of an equivalence theorem can then produce a formula for the optimal design, which can be elusive. Chen el at. (2017) provide examples.

Professor Mong-Na Lo Huang (Huang, et al., 2017) proposed optimal design methodology for group testing experiments, where the goal is to estimate the prevalence of a trait using a test with uncertain sensitivity and specificity. She and her co-authors determined approximate optimal designs for simultaneously estimating the prevalence, sensitivity, and specificity The optimal designs require three different group sizes with equal frequencies. On the other and, if estimating prevalence as accurately as possible is the only focus, the optimal strategy is to have three group sizes with unequal frequencies. Based on a Chlamydia study in the United States, she compared the competing designs and provided Additionally she discussed extensions on budget-constrained optimal group testing designs, where both subjects and tests incur costs, and assays have uncertain sensitivity and specificity that may be linked to the group sizes.

Dr. Stephanie Biedermann (Lee, et al., 2017) described her newly developed methodology for designing experiments when outcome values are not missing at random. This is the first explorative investigation into this topic, with some promising results so far, and thus opens up a new avenue of research on the interface of design of experiments and incomplete data problems, in particular the notoriously challenging situation when missing data are not missing at random. In the ensuing discussion, an interesting modification to the optimality criterion was proposed, which may lead to an increased benefit of the approach in the planning of scientific experiments. Professor Rosemary Bailey described recent work obtaining good block designs for 36 treatments in blocks of size 64, thus filling in a gap in the famous square lattice designs introduced by Frank Yates 80 years ago. Professor Jeff Wu also referred to the ongoing importance of Yates's work in comments on another talk.

Prof Henry Wynn introduced a new optimal design criterion (Kuriki and Wynn, 2017), which can be used to determine an experimental design that minimise the width of simultaneous confidence bands for nonlinear regression models, which are constructed by evaluating the volume of a tube about a curve that is defined as a trajectory of a regression basis vector. Professor France Mentre investigated optimal designs for nonlinear mixed effect models (NLMEM), which are used in longitudinal studies. She reviewed methods evaluating the expected Fisher information based on Monte-Carlo Hamiltonian Monte-Carlo (MC/HMC), which require a priori knowledge on models and parameters, and extended these MC/HMC-based methods to account for uncertainty in parameters and in models.

Professor Min Yang described his recent research into data reduction of big data. Extraordinary amounts of data are being produced in many branches of science. Proven statistical methods are no longer applicable with extraordinary large data sets due to computational limitations. A critical step in Big Data analysis is data reduction. Professor Yang introduced a novel approach called Information-Based Optimal Subdata Selection (IBOSS) for data reduction. The proposed research will open an entirely new avenue for research. It will make a significant contribution by developing methods that extract information from big data more efficiently. The impact will be felt in many areas of science. Existing sampling-based methods face the limitation that the amount of information that they extract is constrained by the subsample size, and does often not increase with the full data size. The proposed IBOSS strategy alleviates this problem. Preliminary results show that the IBOSS strategy retains much more information than the sampling-based methods. During the discussion that followed, the comparison between divide-and-conquer method, and new and unexpected applications of this work to high-dimensional data, such as genomics data were brought forth.

2 Robustness of Design

Suppose that an investigator anticipates planning a study that will result in a number of observations on a random variable Y, whose probability distribution – often merely through its expected value – depends on a vector x of covariates *that can be set by the investigator* – hence the design. After the data are gathered the relationship between Y and x is to be assessed. This will generally involve both estimation and prediction, and is often done in the context of a particular model *of which the experimenter might have only partial knowledge* *and in which he might have little faith* – hence the robustness requirement. 'Robustness' has numerous meanings in statistics. The notion appears to have been introduced by Box (Box, 1953), and was given a firm mathematical basis by Huber (Huber, 1964, 1981), for whom it generally – but certainly not exclusively – meant the relative insensitivity of a statistical procedure to departures from the assumed Gaussian error distribution. In design the usual performance measures depend on the error distribution only through the first two moments, and beyond this the distributional shape is not so relevant. One does however have in mind a particular model to be fitted once the data are gathered. In 'classical' optimal design theory, one believes explicitly that the model one fits is the correct one, and measures the quality of a design through a 'loss function' such as the determinant, or trace, or maximum eigenvalue of the covariance matrix, corresponding to the well known D-, A- and E-optimality criteria. In 'model robust' design theory one instead anticipates that the model that will be fitted by the experimenter is not necessarily the true one – a simple example to bear in mind is that of fitting a straight line regression when the true response function is possibly not exactly linear in the covariate – and so the loss function highlights some more general feature such as the mean squared error (*mse*). This will of course depend on the true, rather than fitted, model and so one seeks a design minimizing some scalar quantity summarizing the increased loss – perhaps the maximum, or average, of the *mse* over the predicted values – as the true model varies. A common framework is that an experimenter plans to fit a particular model to his data, while realizing that any model is at best an approximation. He seeks protection, at the design stage, from increased loss incurred by model mis-specification. Canada has become a noted region of concentration for research in Robustness of Design, through the work of (contact organizer) D. Wiens (Wiens, 2015), with his colleagues and former students, several of whom attended and gave presentations.

Professor Julie Zhou (U. Victoria) presented her recent research on optimal regression designs under the second-order least squares estimator (SLSE). Since the SLSE is more efficient than the least squares estimator when the error distribution in regression model is asymmetric, new optimality criteria under the SLSE have good design properties. An attendee from outside the design community commented on the usefulness of Julie's work to his work, involving the modelling of survival data.

The workshop provided an excellent opportunity for sharing and discussing research ideas. After Professor Mong-Na Lo Huang gave her presentation on optimal group testing designs, Professors Zhou and Huang started to explore possible joint research projects on algorithms for computing optimal group testing designs and robust designs.

In a thought-provoking and elegantly presented address Professor Tim Waite (Manchester U.) proposed usage of minimax efficient random designs based on a frequentist decision-theoretic experimental design approach, with application to model-robust design for prediction. These seem to address in an efficient manner a long open problem – the inadmissibility of a class of design presented by Wiens (Wiens, 1992).

Professor Dave Woods (University of Southampton, UK) presented recent results and ongoing research on sequential design for Bayesian optimisation of physical systems with application to automatic experimentation in the chemical and pharmaceutical sciences. This work, in collaboration with chemists and chemical engineers, aims to develop novel design of experimental methods and apply them in conjunction with automated equipment to increase lab efficiency and reduce costs. A particularly important element of the work is methodology to automatically detect and down-weight potentially outlying observations. Useful feedback from the talk included links to other optimisation methods for maximising expected improvement in computer experiments.

Xiaojian Xu (Brock U.) discussed the effects of maximum likelihood estimation for a generalized linear mixed model (GLMM) when possible departures may appear from its assumed form. The commonly occurring departures involved in a GLMM may include imprecision in the assumed linear predictor, misspecified random effect distribution, or possibly both. She outlined the construction of D-optimal sequential designs which are robust under consideration of these types of departures. Since the computational work involved in GLMMs can be very intensive, an approximate approach was also proposed. Some comparisons were given through simulations.

3 Computer Experiments

The traditional idea of an experiment involves observation of a system of interest under controlled conditions, with the intent of learning something about that system. The system of interest varies by discipline: engineers and physicists may be interested in systems involving physical material, biologists may focus on living organisms (or collections or components of them), while social scientists may be interested in experiments involving the behaviour of human beings. In contrast, the system of interest in a computer experiment is often a computer model, usually a mathematical description of a real system of interest, represented as a computer program. The computer representation is usually necessary due to the complexity of the model. Experimental goals are often similar to those in traditional experiments. While the computer model must, in principle, be fully known, it is generally so complex that a useful understanding of its behavior requires the empirical approach of an experiment (Morris and Moore, 2015).

Computer experiments are increasingly used in many important scientific studies, in part because they can account for the sophisticated correlation structures often found in complex studies that generate very large data sets quickly and continuously, such as in climate changes. For such complicated and expensive physical experiments, a well-designed computer experiment using, say, Latin square designs and sequential designs can reduce the experimental costs significantly. Canada has become somewhat of a hotbed for such work; evidence of this was provided by the attendance of D. Bingham and B. Tang from Simon Fraser University, William Welch from University of British Columbia, Devon Lin from Queen's University and other world leaders in this area, such as Jeff Wu from the Georgia Institute of Technology and Peter Chien from the U. Wisconsin-Madison, together with some of their current and former students.

Professor Will Welch described his recent research into emulation of computer experiments. His talk motivated some to think of new ways to link Gaussian process models with additive correlation functions to general functional additive models. This could lead to a new research direction in emulation. Will pointed out that Gaussian processes (GPs) are widely used for analysis of the input-output relationship(s) of a deterministic computer experiment. While there are many tweaks of the basic model, they turn out to be fairly unimportant for prediction accuracy. In particular, complex input-output functions remain difficult to model with useful accuracy whatever method is used within the usual GP universe of models.

Professor Bingham introduced new types of space-filling designs motivated by several real applications. The proposed designs are unconventional and novel. This is a product of the cross-fertilization between experimental design, combinatorics, and applied mathematics. It shows a new aspect of space-filling designs. The approach was demonstrated on several examples, including the cosmology study of non-linear power spectrum simulation models that motivated the work.

Devon brought 'big data' into focus, via 'fat data' with high dimensional inputs and/or outputs. She proposed a computationally efficient modelling approach to build emulators for large-scale dynamic computer experiments. This approach sequentially finds a set of local design points based on a new criterion specifically designed for emulating dynamic computer simulators. Singular value decomposition based Gaussian process models are built with the sequentially chosen local data. To update the models efficiently, an empirical Bayesian approach was introduced. When a target observation is available, estimating the inputs of the computer simulator that produce the matching response as close as possible is known as inverse problem. She proposed a new criterion-based estimation method to address the inverse problem of dynamic computer experiments.

Professor Jeff Wu described his recent and potentially groundbreaking research into rocket injection design through spatial-temporal modelling; issues on uncertainty quantification were also discussed. He detailed a recent study to illustrate how physics and data are used jointly to learn about the "truth" of the physical world. In the quest for advanced propulsion systems, a new design methodology is needed which combines engineering physics, computer simulations and statistical modelling. There are two key challenges: the simulation of high-fidelity spatial-temporal flows (using the Navier-Stokes equations) is computationally expensive, and the analysis and modelling of this data requires physical insights and statistical tools. In this method, a surrogate model is first presented for efficient flow prediction in swirl injectors with varying geometries, devices commonly used in many engineering applications. The novelty lies in incorporating properties of the fluid flow as simplifying model assumptions, which allows for quick emulation in practical turnaround times, and also reveals interesting flow physics which can guide further investigations. Next, a flame transfer function framework is used for modelling unsteady heat release in a rocket injector. Such a model is useful not only for analyzing the stability of an injector design, but also identifies key physics which contribute to combustion instability. During the discussion that followed, Professor Wu specifically mentioned the importance of computer experiments as well as sequential designs for future developments, especially in industrial applications. This has provided a very good direction for future study on design of experiments.

Professor Peter Chien's talk consisted of three topics on the design and analysis of computer experiments with complex data. The first topic dealt with computer codes with gradients. The gradient-enhanced Gaussian process emulator is widely used to analyze all outputs from a computer model with gradient information. The gradient-enhanced Gaussian process emulator has more numeric problems than in many multivariate cases because of the dependence of the model output and each gradient output. He had derived, and presented, a statistical theory to understand why this problem happens and proposed a solution using a data selection approach. The second topic concerned computer models with invariance properties, which appear in materials science, physics and biology. He proposed a new statistical framework for building emulators to preserve invariance. The framework uses a weighted complete graph to represent the geometry and introduces a new class of function, called the relabeling symmetric functions, associated with the graph. The effectiveness of the method was illustrated by several examples from materials science. The third topic presented a new class of statistical design inspired by the Samurai Sudoku puzzle. These designs have overlapping components and are useful for cross-validating data or models from multiple sources.

4 Advanced Numerical Methods for Searching Optimal Designs

Analytical optimal designs are typically available only for relatively simple models or models with a very special structure, where mathematics can be cleverly applied to find formulas for the optimal designs and to study their properties. With large data becoming increasingly more available and improved modelling techniques, more realistic but more complicated models are employed to draw accurate inference from scientific studies; for example, in fMRI studies on how the brain functions and reacts to different stimuli or how water resources can be better conserved and efficiently utilized by studying the whole water system involving hundreds of variables in hydrology. A focus in the workshop was to develop more efficient numerical methods for finding optimal designs for high dimensional problems. To this end, the workshop promoted cross-disciplinary research by having engineers and computer scientists at the workshop as well. Eminent engineering experts in optimization, as well as current graduate students and recent graduates from statistics programmes, demonstrated how to apply state-of-the-art algorithms, such as nature-inspired metaheuristic algorithms to solve complex design problems.

Professor Luc Pronzato discussed the problem of obtaining good experimental designs for Gaussian process modelling in computer experiments. To determine designs, which have satisfactory space-filling properties he proposed minimax-distance (sub-)optimal designs, which minimise the maximum distance between a point of the region of interest and its closest design point, and thus have attractive properties in this context. As their construction is difficult, even in moderate dimension Professor Pronzato considered several discretisation methods of the experimental region, such as the determination of Chebyshev-centroidal Voronoi tessellations obtained from fixed-point iterations of Lloyds' method, and the construction of any-time (nested) suboptimal solutions by greedy algorithms applied to submodular surrogates of the minimax-distance criterion.

Dr. Seongho Kim, an Associate Professor of Biostatistics at Wayne State University/Karmanos Cancer Institute, described his pioneering developments in pharmacokinetics and phase II clinical trial designs using a stochastic global optimization algorithm, particle swarm optimization (PSO). During his presentation, he brought up three crucial but challenging issues in parameter estimation, global optima, speed of convergence, and statistical identifiability, and demonstrated that PSO is able to deal with those challenges efficiently, leading to the possible opening of a new avenue of research.

Some members of the optimization community attended and gave interesting talks on this important aspect of design construction. In particular, Professor Lieven Vandenberghe from Department of Engineering Departmenat at UCLA described connections between experimental designs and semidefinite programming, and provided up-to-date computing algorithms, useful for finding optimal designs efficiently. Semidefinite programming (SDP) has important applications in optimisation problems that involve moment cones or, by duality, cones of nonnegative polynomials. Examples can be found in statistics, signal processing, control, and non-convex polynomial optimisation. Professor Guillaume Sagnol used semidefinite programming (SDP) and second-order cone programming (SOCP) to compute distributionally-robust (DRO) optimal designs. The distributionally robust approach can be seen as a robust counterpart of the Bayesian approach, where one optimises against the worst-case of all priors belonging to a family of probability distributions. Both these speakers talked about techniques to solving optimization problems not commonly used in the subfield of optimal designs and so attendees are now likely more equipped with additional tools to tackle tough optimization design problems, including high dimensional optimizationa design problems with many covariates.

5 New Researchers

A morning was devoted to presentations from graduate students and recent graduates.

Dr. Rui Hu – a freshly minted Ph.D. – presented her method of constructing robust sampling designs for the estimation of threshold probabilities in spatial studies. Her method, at the design stage, addressed the problem of possible model misspecification when estimating threshold probabilities which are critical in many disciplines such as ecology, epidemiology, etc. This work is a successful application of the theory of robust optimal design and sparked a lot of interest and discussion among participants.

The work presented by Dr. Kirsten Schorning (Feller, et al., 2017) discussed a new field of optimal design theory, namely the construction of optimal designs for several models, sharing some common parameter. Her results have many applications in pharmaceutical investigations where good designs for dose response curves with common parameters are required (for example the placebo effect in daily or twice daily treatment). In particular she determined optimal designs for a recently preformed Phase II clinical trial, where the goal goal was a comparison of two dose response curves corresponding to different treatment groups

A third talk was delivered by Dr. Maryna Prus (Prus and Schwabe, 2016), who investigated optimal design problems for random coefficient regression (RCR) models, which are frequently used in many statistical applications; especially in biosciences and medical research. In the case of multiple group RCR models individuals in different groups get different kinds of treatment and Dr. Maryna Prus determined the optimal group sizes for the prediction of the individual parameters in multi group RCR models with a common population mean for all individuals across all groups.

One of the young researchers scheduled to present at the meeting is Ahipasaoglu Selin from Singapore. She is an Assistant Professor in the Engineering Systems & Design Pillar at Singapore University of Technology and Design since April 2012. She received her doctorate at Cornell University from Prof. Michael Todd in 2009. Afterwards, she worked as a researcher at the Operations Research and Financial Engineering Department in Princeton University and the Management Science Group at London School of Economics. She is interested in Convex Optimization, Sparse Learning, Combinatorial Auctions, and Global Optimization. She is new to optimal design of experiments and was looking very forward to attend and meet top researchers in the field. However, being a Turkish citizen, her visa application was surprisingly denied. The organizers arranged to her present her talk via video and it was very well received. Her talk followed up on Drs. Zhou and Vandenburghe's talks on using semi-definite programming to solve difficult optimization design problems in statistics. She presented a new perspective that many in the audience had not seen before.

6 Special Event

The meeting featured an evening group presentation, with much audience participation, on the Future of Design of Experiements, with presenters Joachim Kunert, Dennis Lin, John Stufken and Boxin Tang, with Rainer Schwabe as moderator and discussant. Joachim emphasized the continuing role of the concepts of blinding, randomization and permutation tests. Dennis shared some of his personal views on the evolution of DOE since R. A. Fisher, and went on to talk about some of his recent work on Design for Order-of-Addition. John asked general questions about our relevance as a group, with suggestions for meeting current challenges. His comments regarding the potential of design of experiments in Big Data inspired comments on the use of such methods in methods – design and analysis – for the IT industry. Boxin took a look at some possible future developments in computer experiments, factorial designs and beyond, through the lenses of optimality, robustness and fusion. Probably more discussion was generated in this session than in any others. Some key topics raised were the need to interact with other disciplines, including computer science, and the need to be involved in big data and data science applications to help ensure scientific rigour through the application of design principles. Comments of Professor Lin regarding our collective and sometimes discouraging methods of statistical nomenclature led to the possible opening of a new avenue of research – 'heartfelt learning' – to exploit methodological links with AI.

Another point that was emphasised in this discussion was the ongoing need for the foundation ideas of experimental design, such as randomisation, replication, blinding and blocking. These are sometimes overlooked in new areas of research. All found the panel on the future of design of experiments extremely insightful. New ideas discussed in the panel, such as subsampling of Big Data, are highly relevant to current research projects and can open new angles to solve those problems.

Some take home messages from the workshop are

- All agreed that design is an important component of many scientific studies and these are well reported and reaffirmed in regulatory and scientific committee reports,
- Researchers in optimal design should work more collaboratively to realize a common goal - greater impact of the subfield of optimal experimental designs in scientific discovery,
- Discussions on how to work strategically to realize the common goal were discussed but there was no clear consensus,
- Some thought that it is increasingly important to do more interdisciplinary work and learn from related disciplines, such as engineering and computer science, in how they solve optimization problems.
- All agreed that the workshop we had at Banff was intellectually stimulating, very helpful in exchanging research ideas and in promoting the subfield of optimal design.

References

G. E. P. Box. (1953). "Non-normality and tests on variances," *Biometrika*, 40, 318-335.

P. Y. Chen, R. B. Chen, and W. K. Wong. (2017). "Standardized maximin D-optimal designs for pharmacological models via particle swarm optimization techniques, " *Chemometrics and Intelligent Laboratory Systems*. In press.

H. Dette, A. Pepelyshev, A. Zhigljavsky (2016). "Optimal designs in regression with correlated errors," *Annals of Statistics,* 44(1), 113-152.

H. Dette, M. Konstantinou, A. Zhigljavsky (2017). "A new approach to optimal designs for correlated observations," *Annals of Statistics,* 45(4), 1579–1608.

C. Feller, K. Schorning. H. Dette, G. Bermann, B. Bornkamp (2017). "Optimal designs for dose response curves with common parameters," *Annals of Statistics,* In press.

S. H. Huang, M.-N. L. Huang, K. Shedden, W. K. Wong (2017). "Optimal group testing designs for estimating prevalence with uncertain testing errors," *Journal of the Royal Statistical Society, Ser.B,* In press.

P. J. Huber, (1964). "Robust estimation of a location parameter, " *The Annals of Mathematical Statistics*, 35, 73-101.

P. J. Huber, (1981). *Robust Statistics*, Wiley.

S. Kuriki, H. P. Wynn (2017). "Optimal experimental design that minimizes the width of simultaneous confidence bands," arXiv 1704.03995.

K. M. Lee, R. Mitra, and S. Biedermann. (2017) "Optimal design when outcome values are not missing at random, " *Statistica Sinica*. In press.

M. D. Morris and L. M. Moore. (2015). Design of Computer Experiments: Introduction and Background, In *Handbook of Design and Analysis of Experiments,* 577–591, CRM.

M. Prus and R. Schwabe (2016). "Optimal designs for the prediction of individual parameters in hierarchical models," *Journal of the Royal Statistical Society, Ser.B,* 78, 175–191.

D. P. Wiens, (1992). "Minimax designs for approximately linear regression, " *Journal of Statistical Planning and Inference,* 31, 353–371.

D. P. Wiens, (2015). "Robustness of Design. In *Handbook of Design and Analysis of Experiments,* 719–754, CRM 2015.