Optimal Bayesian Design of Experiments for Polymerization Processes:

I. Implementation to Nitroxide-Mediated Radical Polymerization (NMRP)

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General Research Objectives

- Apply ideas from design of experiments (applied statistical methodology) to various polymerization processes to:
  - Identify optimal operating conditions to achieve certain polymer properties
  - Clarify/determine values of key kinetic parameters of related process models

Why Bayesian Design?

- Experimental flexibility
  - No restrictions in number of experiments, sequence of experimentation, factor levels, dropping/adding factors, etc.
- Requires fewer trials
- **But** mainly, it does not ignore/discard prior knowledge
  - Prior information is updated in a sequential manner, thus allowing, in parallel, the optimal update of key unknown parameters
  - Prior information involves contributions from both the prior experimental region and a (usually non-linear) mathematical model for the process, thus making use of both experimental information and mechanistic models

Why Bayesian Design in NMRP?

- Although literature on NMRP extensive, still many conflicting statements
- Many mechanistic claims, based on only a few data points over a typical 50 hr polymerization period
- Modeling efforts sporadic and usually very "case-specific"
- Design of experiments and systematic, concerted efforts lacking

Procedure for Bayesian Design of Experiments

3. Select the "best" experiments using a search algorithm
4. Analyze the experiments
5. Update the prior variance/covariance matrix (U) and vector of parameter estimates (θ)
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4. Analyze the experiments
5. Update the prior variance/covariance matrix (U) and vector of parameter estimates (θ)
6. Given the new variance/covariance matrix, select the next sequence of experiments. Analyze the experiments and update θ and U, accordingly
7. Repeat step 6 until the final sequence; select the last sequence of "optimal" experiments; after the analysis of the experiments, update the vector of the parameters, for the last time

A Sample of Results : NMRP Case Study

- Choose design factors and their levels
  - based on a detailed and critical analysis of literature

Ingredient	Amount (Low)	Amount (High)
T (°C)	120 °C	130 °C
$[I]_0$ (M)	0.036	0.072
$[N]_0$ (M)	0.058	0.082

$[I]_0$: initial initiator concentration (BPO); $[N]_0$: initial nitroxide concentration (TEMPO)

- Selection of responses
  - Batch time
  - Weight-Average Molecular Weight
- Incorporation of prior knowledge
  - To generate the prior : 2^3 conventional factorial design was simulated with a computer program based on a general mechanistic model developed for NMRP
  - Linear regression on the data : vector of parameter means
  - "Brainstorming" on the maximum/minimum value of the parameters: variance
- Variances of the responses were calculated from previous experimental results and experience
- Selection of experimental design
  - Two sequences of two experiments
  - Objective: quantify the relative importance of key factors

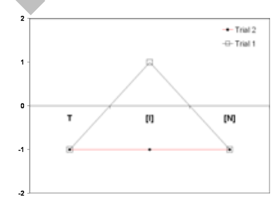

Illustration of the first sequence of experiments

- Variance/covariance matrix and the vector of parameter means were updated
- Next sequence of two experiments was designed using the updated variance/covariance matrix

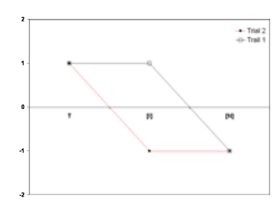

Illustration of the second sequence of experiments

Discussion

- To quantify the relative importance of the parameters as well as the adequacy of the model used to generate the "prior knowledge", certain statistical tests were carried out
- **Test 1**: indicator of the "uncertainty of the expert"
- **Test 2:** indicator of the actual significance of an effect
- **Test 3:** indicator of the "quality of expert's opinion"
- Results and tests for molecular weight response of case study

[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
T×[I]	-183.40	-173.95	-183.40	-1.83	-1.84	5.88E-05
T×[N]	107.10	106.98	107.04	0.11	0.19	-0.0001
[I]×[N]	-175.13	356.79	498.44	-0.23	1.15	1.54871
T×[I]×[N]	140.23	137.86	140.23	2.80	2.81	-2.9E-05
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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  - TEMPO concentration, [N], is most influential on molecular weight response
  - Effect of temperature on molecular weight response is not that dramatic in this range (Effect of initiator concentration, [I], as expected)
  - Test 1 shows that all three main factors are **significant** in expert's opinion
  - Test 2 verifies the actual **significance** of an effect; in agreement with expert's opinion
  - Test 3 implies that expert's opinion is valid; the mechanistic model seems reliable
  - Bayesian analysis in case study has confirmed/reinforced experimental results!

Future Work

- Expand the implementation of Bayesian design in NMRP by using a non-linear model
- Combine the Bayesian design methodology with statistical criteria to reduce parameter correlation
- Bayesian technique perfectly general; can be potentially applied to other processes
  - Examples: Emulsion copolymerization of NBR/ SBR rubber; NMRP in supercritical carbon dioxide; Multi-component polymerization systems with depropagation; NMRP in the presence of cross-linking, etc.