Reactivity Ratio Estimation for the VBK and MMA Free Radical Copolymerization System Using the EVM Framework: From preliminary estimation to optimal design - the Five Ws -

Niousha Kazemi, Benoit Lessard, Thomas A. Duever, Alexander Penlidis

This extended abstract summarizes the five *Ws*- the who, what, why, when, and where' questions than need to be addressed to understand the necessity of using the Error-in-Variables-Model (EVM) framework for determining reactivity ratios in multicomponent polymerization systems.

Who might benefit from the Error-in-Variables-Model (EVM) framework?

Polymer researchers from both academia and industry are well aware of the importance of polymerization kinetic studies. Kinetic modeling studies are key to understanding the underlying nature of polymerization reactions and therefore absolutely essential for working with new materials and tailored-made properties for polymeric products. Reactivity ratios for multicomponent polymerization systems represent such crucial pieces of information and thus many researchers have spent time and effort over many years to determine these parameters, albeit with conflicting results.

What is missing from past studies in reactivity ratio estimation?

For the purpose of reactivity ratio estimation in copolymerization systems, there have been numerous publications in the literature over the past 60 years, during which two main approaches have largely been implemented and thus established as the commonly used solutions for the problem of estimating reactivity ratios. These two methodologies, indicated below, can both become sources of unreliability in reactivity ratio estimates. The first and main practice is to use low conversion experimental data with the instantaneous copolymer composition model (a.k.a, the Mayo-Lewis model). This model, similar to many other polymerization models governing these phenomena, is nonlinear in its parameters; yet, the majority of reactivity ratio estimation studies have been (and still are) treated with linear estimation approaches and often graphical techniques. Moreover, this model is only applicable to low conversion data, based on several unrealistic assumptions. Consequently, there are many poor and biased reactivity ratio estimates reported in the literature, as has repeatedly been indicated in the past (e.g., see Dube et al. (1991) and Polic et al. (1998)).

The second approach, commonly practised among polymer chemists, is to perform experiments covering a broad range of feed compositions (the so-called empirical approach), believing that such an approach would provide a large number of experimental points and hence the best results for estimating reactivity ratios. Even though design of experiments (DOE) approaches for obtaining improved reactivity ratios have been proposed since the mid-60s (notably by Tidwell and Mortimer (1965)), empirical approaches have dominated and are readily used by almost all researchers, often slightly modified, but mainly far from any optimality consideration, with largely unreplicated collection of experimental data. Looking in depth at these issues, it can be realized that most of the existing and published approaches in this field suffer from oversimplifications and/or violation of certain underlying estimation and experimental assumptions.

Why should the EVM framework be implemented for this problem?

This whole area requires a complete overhaul with respect to employing "state of the art" parameter estimation approaches and design of experiment strategies. A relatively recent approach is the Error-in-Variables-Model (EVM). EVM represents the most complete approach for situations where the dependent and independent variables do not need to be distinguished. In general, EVM is capable of handling linear and nonlinear, single- and multi-response problems, and has several advantages. It treats each measurement as an unknown true value plus an error term; thus, one is compelled to consider errors involved in all the data. If nothing else, EVM forces one to think about errors and error structure. These features have prompted the application of the EVM method for estimating reactivity ratios in multicomponent polymerization systems and, over the course of the past decade, reactivity ratio estimates from this method have increasingly been appearing in the literature (for example, see Kazemi et al., 2011).

For parameter estimation purposes, early attempts in implementing the EVM method for determining monomer reactivity ratios were generally at low conversion levels using the Mayo-Lewis equation, owing to the assumption that the composition drift in the monomer feed is negligible at low conversion levels. However, many copolymerization reactions will inevitably show compositional drift as the degree of conversion increases. Alternatively, a direct step-by-step integration of the copolymerization composition ordinary differential equations (also referred to as DNI, Direct Numerical Integration approach) allows us to utilize medium and high conversion data points for estimating reactivity ratios. This approach can significantly improve the quality of the results by including more information in the analysis as well as avoiding limitations of collecting low conversion data (sources of errors). The performance of this approach in comparison with the Mayo-Lewis model as well as some other proposed methods were evaluated and discussed in detail in Kazemi et al. (2011). Consequently, the EVM framework is completely based on the DNI approach, and it can handle experimental data of any conversion level.

For the design of experiments (DOE), on the other hand, which is a crucial part of any parameter estimation study, the basic idea is to select experimental trials which minimize variability in the parameter estimates (which is, in its turn, related to the variance-covariance matrix of the parameter estimates). The combination of an efficient and reliable parameter estimation technique with informative data obtained from designed experiments can offer significant improvements on the quality of the estimated parameters. The influence of designing experiments has briefly been discussed in the literature for the problem of reactivity ratio estimation, yet rarely practised. The D-optimal criterion, perhaps the most common criterion used in the literature for obtaining improved parameter estimates, aims at minimization of the determinant of the variance-covariance matrix of the parameters. The D-optimal design criterion assumptions, however, might be violated if there is error in all variables (i.e., EVM structure). The difference between the EVM context and the traditional nonlinear regression analysis is how they treat errors in the variables involved. **Hence, if a parameter estimation problem, and hence the related DOE procedure, should be studied by the EVM method, using traditional nonlinear regression DOE techniques (like classical D-optimality) may lead to unreliable results.**

Although the basic EVM equations and parts of the EVM algorithm applied to several nonlinear parameter estimation problems have appeared before in such papers as Reilly and Patino-Leal (1981), Dube et al. (1991), Reilly et al. (1993), and Polic et al. (1998), they appeared in a rather fragmented way and certainly not all of them in one source, traversing the full spectrum from the design of experiments all the way to parameter estimation and diagnostic checks. In our recent publications, Kazemi et al. (2013a, 2013b), it has been shown that implementing the EVM framework increases the precision of reactivity ratios compared to many other existing methods; also,

using the optimal design criterion within the EVM context optimizes the efficiency of this procedure and leads to most reliable reactivity ratios (of better quality compared with inappropriately designed trials).

When should we start and stop?

The EVM framework combines the parameter estimation and design of experiments procedures, along with further strategies that customize this framework for the context of the reactivity ratio estimation problem. This approach, when practised within the EVM context, has the potential to increase the reliability of the reactivity ratio for any copolymerization system (an example is shown in the next section). Also, these steps can be implemented on investigations of any larger multicomponent polymerization. The following steps summarize the guidelines of this methodology in a practical way.

Step 1: Reactivity ratio estimation from preliminary experiments

Since design of experiment methods for nonlinear models need initial guesses for the parameters, the starting point in studying reactivity ratios of any copolymerization systems is to find preliminary values for reactivity ratios either from the literature or by performing screening experiments. These experimental results should then be analyzed with the DNI approach for estimating reactivity ratios.

Step 2: Design of experiments: Initial design

Generally, there are two approaches for model-based DOE, namely, initial and sequential design. The initial design refers to the problem where no prior information is available and the objective is to design the first data set to permit parameter estimation. Most of the practice for design of experiments for the purpose of parameter estimation has been focused on the initial design scheme, where no previous experimental information is considered, except for preliminary reactivity ratio values. It is desired to determine what set of experiments to perform so as to provide the most information about the unknown parameters (hence, initial design). Based on the initial reactivity ratio values, mentioned in step 1, initial optimal feed compositions (for further experimentation) are obtained by the EVM design criterion, based on experimentally feasible regions.

Step 3: Performing full conversion experiments and re-estimating reactivity ratios

The results from the initial design of experiments for copolymerization systems are two optimal feed compositions. For each designed initial feed composition, experimental data on copolymer composition are collected at conversion levels such as 5%, 10%, …, 60%, and 70% (higher conversion, if possible). All these data points, in terms of their initial feed compositions, conversion values, and their cumulative copolymer compositions are analyzed with the DNI approach. The reactivity ratio estimates are then reported along with their corresponding joint confidence region that reflects their level of uncertainty. If these results show adequately reliable values (point estimates), the procedure can be stopped. If, on the other hand, further improvement is needed, then step 4 should be considered.

Step 4: Design of experiments: Sequential design

The sequential design problem, as opposed to the initial design scheme, applies to the case where parameter estimates and some data from previous (designed or not) experiments are available, but the parameters have not yet been estimated with sufficient precision. In this scenario, after having conducted a set of n experiments, it is desired to find the optimal location of the next experiment(s) which can increase the precision of the results. Even though using any optimal design compared to an empirical design (arbitrary design, e.g., equally spread points covering the variable range), enhances the amount of information for the subsequent analysis (i.e., parameter

estimation), the sequential design scheme has the potential of improving the results even further. Utilizing prior information into the sequential design increases the information content considerably, and thus the reliability of the results.

Finally, it must be noted that how far this procedure should be pursued and the question of "when to stop" have to be answered with the desired magnitude of error in the final results in mind (e.g., the level of tolerance dictated by the target application).

Where can this approach be applied?

Herein, the implementation of the EVM framework for estimating the reactivity ratios of a new, largely unstudied and novel copolymerization system, 9-(-4-vinylbenzyl)-9H-carbazole (VBK) and methyl methacrylate (MMA), is illustrated. Investigation on these reactivity ratios has been initiated by Lessard et al. (2011), where preliminary attempts to study the reactivity ratios of this system were done by performing low conversion experiments and using a nonlinear regression fitting procedure to estimate the reactivity ratios. These reactivity ratios with their confidence intervals are shown in Figure 1. Due to the significance of these reactivity ratios in the application of this copolymerization system, collaborative work was undertaken in order to further analyze these reactivity ratio values and improve their reliability and precision using the EVM framework.

The low conversion data in Lessard et al. (2011) were used as the preliminary experiments and the reactivity ratios were estimated using the DNI approach. These reactivity ratios were then utilized to calculate initial optimal feed compositions (DOE step). Since there are two reactivity ratios under study, two optimal feed compositions, $f_{VBK,1}$ and $f_{VBK,2}$, should be located. The values of these points depend on the (initial or prior) values of reactivity ratios. Based on these prior values the EVM design criterion resulted in two feed compositions, one close to zero and a second one at a larger mole fraction. In order to keep the design procedure optimal and practical, the lower value of $f_{VBK,1}$ should be the lowest limit of the feasible region that is determined for each system based on operating conditions and experimental settings. Therefore, in this case, feed compositions of $f_{VBK,1}$=0.04 and $f_{VBK,2}$=0.30 were selected as initial optimal experiments. Experiments were subsequently run up to medium conversion (~ 60%) and were independently replicated.

Using the initial optimal data set, the reactivity ratios were re-estimated and the results are also shown in Figure 1. As can be seen from Figure 1, the non-designed reactivity ratios (Lessard et al., 2011) are not very close (statistically speaking) to the new reactivity ratios. Another, more interesting, observation is that the new reactivity ratios exhibit a joint confidence region (JCR) that is considerably smaller than the one based on the original data. These results were expected as the optimally designed experiments are supposed to provide the best set of observations for the purpose of parameter estimation and therefore, the point estimates would show less amount of uncertainty (smaller JCR). This part of the analysis clearly proves our point that implementing the EVM framework increases the certainty of the results and, in turn, our appreciation and understanding about the true values of these reactivity ratios.

To increase the precision of these reactivity ratios further, an optimal feed fraction for a sequentially designed experiment was also calculated using the information obtained from the initially designed experiments. The optimal feed composition for the next sequential experiment was at $f_{VBK,next}$=0.45. The new trial was performed and the results were added to the initial optimal data to re-estimate the reactivity ratios. The results are shown in Figure 1 as well. Based on the results in Figure 1, it can be clearly seen that, including the next sequential experiment, resulted in the smallest JCR (i.e., the most precise reactivity ratio estimates amongst all analyzed cases). The new values were in complete agreement with the previously obtained optimal reactivity ratios. For all these designed cases, the sizes of JCRs are considerably smaller than JCRs obtained from initially non-designed

experiments, validating our premise that performing optimal experiments improves the quality of reactivity ratios, thus making it a very useful step in the overall process of determining reliable reactivity ratios.

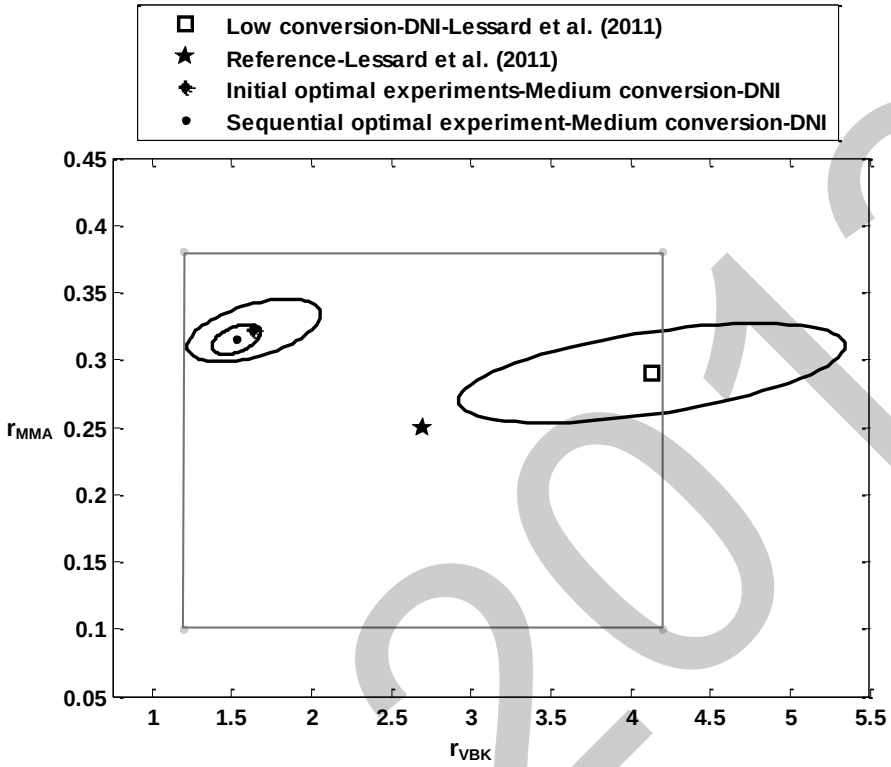

Figure 1. Reactivity ratio estimates and their JCRs for VBK/MMA copolymerization

Finally, it is instructive to note that the rise in reliability of point estimates from designed experiments indicates the portion of replication needed for the non-designed experiments to achieve the same precision for the reactivity ratios as for the sequentially designed ones, and thus the relative time, effort, and cost of working through inaccurate techniques. This example gives a clear and strong experimental verification for the cases where the EVM framework should become a commonly practised procedure for determining reactivity ratios with the highest possible level of confidence.

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Reactivity Ratio Estimation using the EVM Framework

How to obtain optimal estimates

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Reactivity ratios in multicomponent polymerization

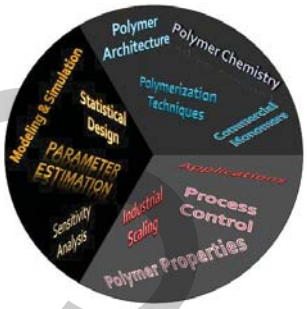
Important aspects in polymer design:

polymer chemistry, modeling and simulation, polymer properties

Reactivity ratios: Important parameters in polymerization kinetics

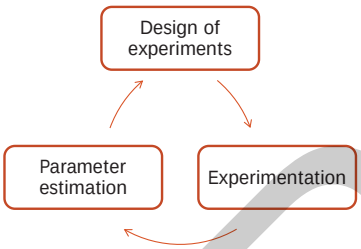
- Physico-chemical nature of the polymerizing system

Having accurate reactivity ratio values is of outmost importance.



Research Objectives

Develop a general framework for applying correct statistical procedures to obtain the most reliable reactivity ratio estimates



Within

the Error-in-Variables-Model (EVM) context…

EVM framework

***Who* might benefit from the EVM framework?**

***What* is missing from past (or current!) studies?**

***Why* should the EVM framework be implemented?**

***When* should we start and stop?**

***Where* can this approach be applied?**

***How* can this approach be applied?**

Poster presentation

Who …

Polymer researchers from ***academia,***

- ✓ underlying reaction kinetics
- ✓ chain microstructure
- ✓ general prescriptions for obtaining reliable parameter estimates

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and ***industry***,

- ✓ reliable database for developing new materials
- ✓ maximize the information obtained from each experiment
- ✓ minimize the number of analyses, cost and time required

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What is missing…

Reliable statistical procedures for reactivity ratios estimation

- Statistically incorrect and outdated procedures
- Collecting data at only low conversion levels
- Large discrepancies and inconsistencies in databases for reactivity ratios

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Adequate and informative experimental data

- Experiments are poorly (if at all) designed
- Limited operating regions and unreplicated experiments

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Error-in-Variables-Model (EVM)

- EVM consists of two statements:

  Equating the vector of measurements ($\underline{x}_i$) to the vector of true values

  $$\underline{x}_i = \underline{\xi}_i^{*}(1 + \underline{\varepsilon}_i)$$

  The true values of the parameters (θ^*) and variables ($\underline{\xi}_i^{*}$) are related with the model

  $$g\left(\underline{\xi}_i^{*}, \theta^*\right) = 0$$

- EVM objective function

  $$\phi = \frac{1}{2}\sum_{i=1}^{n} r_i \left(\bar{x}_i - \hat{\underline{\xi}}_i\right)' \underline{V}^{-1} \left(\bar{x}_i - \hat{\underline{\xi}}_i\right)$$

- EVM is the perfect method for estimating reactivity ratios

Design of Experiments

- Minimize uncertainty in the estimated parameters
- Tidwell – Mortimer (1967) design criterion

  $$f_{21} \cong \frac{r_1}{2+r_1} \qquad f_{22} \cong \frac{2}{2+r_2}$$

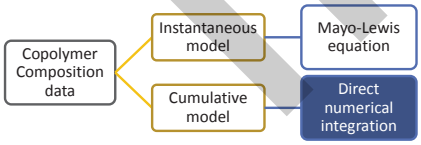
  - D-optimal design criterion
  - Min (|variance-covariance matrix|) or Max (|information matrix|)
  - Conflict with nature of reactivity ratio estimation problem
- EVM information matrix

  $$\underline{G} = E\left[\frac{d^2\phi}{d\theta_i d\theta_j}\right] = \sum_{i=1}^{n} r_i \underline{Z}_i' \left(\underline{B}_i \underline{V} \underline{B}_i'\right)^{-1} \underline{Z}_i$$

  $$\underline{B}_i = \left[\frac{\partial g\left(\underline{\xi}_i, \underline{\theta}\right)}{\partial \underline{\xi}_i}\right] \qquad \underline{Z}_i = \left[\frac{\partial g\left(\underline{\xi}_i, \underline{\theta}\right)}{\partial \underline{\theta}}\right]$$
- EVM design criterion

  $$Max_{\xi} \left|\left[\sum_{i=1}^{n} \underline{Z}_i' \left(\underline{B}_i \underline{V} \underline{B}_i'\right)^{-1} \underline{Z}_i\right]\right| \text{ subject to } \begin{cases} g\left(\hat{\underline{\xi}}_i, \underline{\theta}\right) = 0 \\ L \le \underline{\xi}_i \le U \end{cases}$$

Direct Numerical Integration (DNI)



$$\frac{df_1}{dx_n} = \frac{f_1 - F_1}{1 - x_n} \longrightarrow \bar{F}_1 = \frac{f_{10} - f_1(1 - x_n)}{x_n}$$

$$F_1 = \frac{r_1 f_1^2 + f_1 f_2}{r_1 f_1^2 + 2 f_1 f_2 + r_2 f_2^2}$$

- ✓ Not limited to low conversion data only
- ✓ Properly accounting for the effect of compositional drift
- ✓ Successful over the full conversion trajectory

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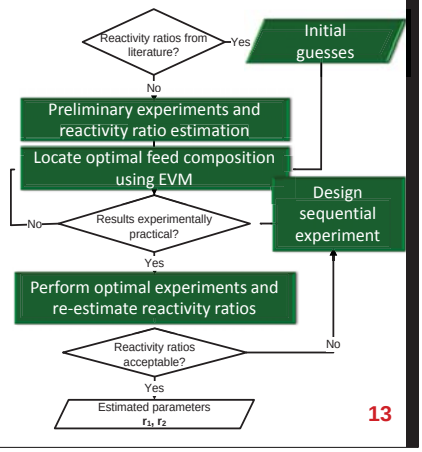
***How* can this approach be applied?**

From Start to Finish

- Preliminary reactivity ratio estimation
- Design of Experiments: Initial design
- Performing full conversion experiments
- Design of Experiments: Sequential design



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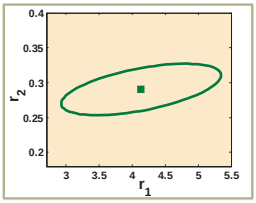
An Experimental Case Study (novel, unstudied)

9-(4-Vinylbenzyl)-9H-Carbazole (VBK, M_1)
Methyl Methacrylate (MMA, M_2)

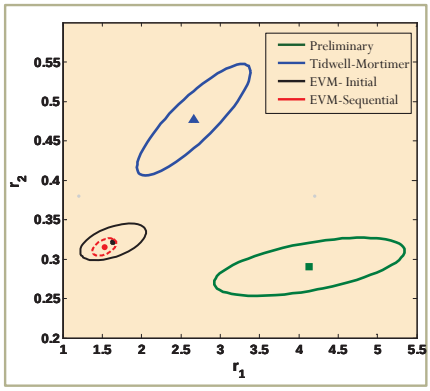
- Preliminary reactivity ratios
  - × No design
  - × Low conversion data
- Initial design of experiments
  - ✓ Tidwell-Mortimer criterion
  - ✓ EVM design criterion
  - ✓ Low VBK compositions



	$f_{1,1}$	$f_{1,2}$
Tidwell and Mortimer	0.13	0.33
EVM	0.04	0.30

VBK-MMA Copolymerization

- ✓ Higher precision for designed experiments
- ✓ EVM vs. Tidwell-Mortimer design criteria
  - ✓ *First ever comparison*
  - ✓ *EVM results are more reliable*
- ✓ Sequentially designed optimal experiments improved the precision even further
- ✓ The investigation has reached an acceptable level of reliability



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Poster presentation

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Questions?

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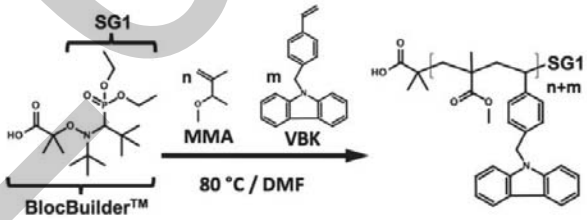
Back-up slides….

VBK/MMA copolymerization reaction



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