Adaptive Repeated Measures Modeling Using Likelihood Cross-Validation

ABSTRACT
An approach for exploratory repeated measures modeling is presented, based on adaptively selected fractional polynomial models for the expected outcome value combined with the standard compound symmetry covariance structure for representing within-subject dependence. The search strategy for identifying an appropriate model for the expected value is based on likelihood cross-validation scores together with tolerance parameters specifying how much of a change in those scores can be tolerated. These methods extend existing adaptive regression methods for uncorrelated situations to correlated outcomes settings. They also serve as a test case for development of methods to handle more general covariance structures. Example analyses are presented using longitudinal data on self-reported adherence to antiretroviral medications for HIV positive subjects.

KEYWORDS
Adaptive modeling, likelihood cross-validation, longitudinal data, medication adherence, nonparametric regression, repeated measures

1. Introduction

When outcome (response, dependent) variables are repeatedly measured under different conditions for the same subject within a research study, the standard statistical model involves a general linear model for the expected outcome value together with compound symmetry covariance [1]. The model for the expected outcome is based on standard parametric approaches like regression, analysis of variance, or analysis of covariance. The assumed covariance structure has constant correlations between outcomes measured under different conditions as well as constant variances, and so is called compound symmetry or exchangeable correlations.

Research studies formulate specific models for expected outcome values prior to data collection to address hypotheses underlying the specific aims of those studies. Once study data are collected, however, it becomes possible to do more than test study hypotheses. Exploratory modeling of available outcomes can provide deeper understanding of relationships within the data and suggest hypotheses for future studies. This can involve searching through substantial classes of models, e.g., arbitrary numbers of arbitrary power transforms of numeric variables, requiring adaptive search strategies to identify models appropriate for the data under analysis. This paper presents a method for adaptively searching through regression models for the expected value of repeatedly measured outcomes under the standard compound symmetry covariance structure. The search strategy employed here was formulated by Knafl et al. [2] to handle the general univariate outcome context. While their analyses focused on Poisson regression for counting outcomes, their approach applies as well to linear and logistic regression with continuous and categorical univariate outcomes, respectively. Thus, this paper extends prior work on univariate outcomes to handle multivariate outcomes. It focuses on continuous outcomes with compound symmetry covariance, serving as a test case for extension of these methods to handle other types of covariance structures and other types of outcomes as well as for the development of methods for searching through alternative covariance structures.

2. Modeling

2.1. Repeated measures models

Suppose that repeated measurements of an outcome variable $y$ have been taken for subjects of a research study indexed by $s$ in $S=\{1,2,\ldots,n\}$ over some subset $C_s$ of conditions indexed by $c$ in $C=\{1,2,\ldots,r\}$. While researchers attempt to measure each subject at all $r$ repeated measurement conditions, in practice, this is unlikely to hold for all subjects, hence the need for the subsets $C_s$ of $C$ to account for such partial outcome situations. The conditions $c$ might be multi-dimensional, e.g., when they correspond to combinations of different family members and time points, but can always be mapped into the integer index set $C$.

Let $y$ denote the vector of all $r$ possible repeated measurements for a subject, with entries $y_c$ for $c$ in $C$. Consider $y$ to be multivariate normally distributed with expected value the vector $\mu$ having entries $\mu_c$ for $c$ in $C$ and with covariance matrix $\Sigma$ having entries $\Sigma_{cc'}$ for $c$ and $c'$ in $C$. Let $y_s$ denote the vector of available measurements for subject $s$ with entries $y_{cs}$ for $c$ in $C_s$. This is then also multivariate normally distributed, but with expected value $\mu_s$ and covariance matrix $\Sigma_s$ obtained by restricting $\mu$ and $\Sigma$ to the indexes in $C_s$. That is, $\mu_s$ has entries $\mu_c$ for $c$ in $C_s$ and $\Sigma_s$ has entries $\Sigma_{cc'}$ for $c$ and $c'$ in $C_s$. Let $L_s(\mu, \Sigma)$ denote the likelihood term for the vector $y_s$ of outcome values for subject $s$ so that the associated log likelihood term satisfies
In many situations, the predictors underlying the fixed component are based on specific parametric linear models, as in the case of testing study hypotheses specified prior to data collection. Exploratory mixed modeling, on the other hand, involves consideration of alternative fixed and/or random components. Nonparametric regression involves classes of fixed component models based on alternative predictor matrices \( X \) with unbounded column dimension. For example, the fractional polynomial class used in reported analyses considers \( X \) matrices based on arbitrary numbers of arbitrary powers of given variables \( t \) like time in the study. For nonnegative \( t \) like time, zero values cannot be raised to negative powers, so only positive values of \( t \) are transformed while zero values are left as zero. Hence, the transform for power \( q=0 \) corresponds to the step function with value \( 0 \) at \( t=0 \) and value \( 1 \) at all observed \( t>0 \).

### 2.2. Likelihood cross-validation

For any nonempty subset \( S' \) of \( S \), denote by \( \hat{\beta}(S';RC) \) the FIML estimate of \( \beta \) computed from data for subject indexes in \( S' \), under an arbitrary random component RC, and by \( \hat{\Sigma}(S';RC) \) the FIML estimate of \( \Sigma \) for that same subset of indexes. Let \( F_h \) for \( 1<h<k \) denote k folds that partition \( S \) into nonempty subsets with nonempty complements \( F_h^c\setminus SF_h^c \). Denote by \( F_h^c \) the unique fold containing the subject index \( s \). The contribution to the likelihood cross-validation (LCV) score for the \( s \)-th subject is given by the likelihood for that subject evaluated at parameter estimates computed from data for subject indexes not in the same fold as \( s \). In other words, it is the deleted likelihood term

\[
\text{LCV}_s = \log(L(\hat{\beta}(F_h^c;RC), \hat{\Sigma}(F_h^c;RC)))
\]

with associated deleted log likelihood term

\[
\log(\text{LCV}_s) = -e_s(F_h^c;RC)\Sigma^{-1}(F_h^c;RC)e_s(F_h^c;RC)/2 - \log(|\Sigma(F_h^c;RC)|)/2 - \log(2\pi)/2
\]

where \( e_s(F_h^c;RC) = y_s - X_s\hat{\beta}(F_h^c;RC) \) is the associated deleted residual vector. The LCV score

\[
\text{LCV} = \prod_{s=1}^{m} \text{LCV}_s
\]

is then obtained by combining these deleted likelihood terms over all subjects, where \( m=r_1+\ldots+r_n \) is the total number of measurements for all subjects. It is sufficient to just multiply the individual LCV terms, but taking \( m^n \) roots means that LCV scores are geometric average deleted likelihoods and so are comparable across data sets with differing numbers \( n \) of outcome measurements. Models with larger LCV scores are better models with better predictive capability and more compatible with the available data as measured through deleted predictions determined by the fold assignment.

A fold assignment mechanism is required to allocate subjects to folds. The analyses of Section 3 use random fold assignment, i.e., subjects are assigned to folds when uniform fold assignment variables take on values within associated fixed ranges partitioning \((0,1)\) into \( k \) disjoint equal-size intervals. The same initial seed is used in computing LCV scores for different models for the same data so that those scores are comparable.

This cross-validation formulation utilizes subject-wise
deletion, i.e., all measurements for a subject are deleted simultaneously, the standard approach used in repeated measures situations. For example, Lee [7] uses subject-wise deletion for growth curve modeling. Measurement-wise deletion can also be used, deleting folds chosen from among the m measurements rather than the n subjects, but consideration of this alternative, nonstandard deletion approach is outside the scope of this paper.

A fixed choice for the number k of folds is commonly used. For example, 10 folds were used in [2] based on the recommendation in [8]. However, the appropriate value for k will likely change with the size of the data set, which in the multivariate outcome setting involves the number m of measurements, not just the number n of subjects. Alternate choices for k are considered in Section 3.2 to assess the impact of that quantity on the results.

### 2.3. Adaptive fixed component model selection

For a fixed choice RC for the random component, an adaptive choice for the fixed component can be obtained by searching through a specific class of alternate predictor matrices X to obtain a choice with a reasonably good LCV score relative to other predictor matrices under consideration. The predictor matrix with the best overall LCV score need not be the best choice; it might include extraneous terms (columns) providing negligible improvements. A possible alternative approach is to allow a limited reduction in the LCV score to obtain a more parsimonious model.

Considerations like this form the basis for the rules controlling the heuristics for searching through alternative models described in [2]. This search proceeds through two phases, an expansion starting from a base model (often the constant model with only an intercept) followed by a contraction. The model produced by the expansion is the base model of the contraction. All terms of the model including the intercept are subject to removal in the contraction. The selected model is the one generated by the contraction. This process is similar to standard variable selection procedures applied to a fixed set of transforms. The expansion is analogous to forward selection while the contraction resembles backward elimination. However, each expansion step considers any possible power transform to add to the model, rather than just those in a fixed set. Moreover, model transforms have their powers adjusted with each contraction step. The process also differs from stepwise selection in only contracting after the expansion ends rather than after each expansion step. The goal of this search process is to obtain a parsimonious model with a nearly optimal LCV score. Such models are preferred to models with optimal scores if optimality is achieved through inclusion of extraneous terms.

Rules are used to guide the model selection, since exhaustive search is impractical, controlled by percent changes in LCV ratios. Tolerance parameters control the rules, e.g., the expansion and contraction phases stop when percent changes in LCV ratios first exceed specific tolerances. Recommended settings for these parameters are provided in [2] that typically produce models with highly significant coefficients, usually selecting parsimonious models, i.e., with all selected predictor variables providing substantive predictive benefits (as measured by substantive decreases in LCV scores with those variables removed from the model). However, the contraction stopping tolerance parameter \( \tau_{CS} \) may require adjustment to avoid removal of valuable terms from the model, especially as the number m of measurements increases. Smaller \( \tau_{CS} \) values can also substantially reduce the computations for large numbers of measurements as in reported analyses. Consequently, \( \tau_{CS} \) was set to 0 to speed up processing, except when explicitly adjusted in an analysis, but all other tolerance parameters are set to their recommended values.

### 2.4. Alternating component selection

The search techniques of Section 2.3 have previously been evaluated only in the univariate outcome setting (with only one outcome per subject, \( r=1 \)), but they apply as well to multivariate outcomes settings with a fixed choice for the random component RC. They can, however, require substantially more computation depending on the complexity of RC. For this reason, the following strategy, alternating between computing an adaptive fixed component and estimating the parameters of the random component, is proposed for reducing the computational effort and is investigated in Section 3.3.

Step 0. For the initial model of the search (with only an intercept term), compute the estimate \( \hat{\beta}_0 \) of the parameter vector \( \beta \) for RC (but only CS is considered in Section 3.3 for simplicity) as well as the associated estimate of \( \hat{\beta} \). Step 1.A. Hold the parameter vector \( \hat{\beta}_0 \) fixed at \( \hat{\beta}_0 \) or some subset like all but a homogeneous variance parameter) throughout the adaptive search, computing estimates \( \hat{\beta}(S; RC(\hat{\beta}_0)) \) of \( \hat{\beta} \) for alternative choices for \( X \) and generating an adaptive choice \( X(\hat{\beta}_0) \). Step 1.B. Compute the estimate \( \hat{\beta}_1 \) for the model based on \( X(\hat{\beta}_0) \) as well as the associated estimate of \( \hat{\beta} \) with score LCV(\( X(\hat{\beta}_0)\),\( \hat{\beta}_0 \)).

Step 2.A. Using \( X(\hat{\beta}_0) \) as the base model and holding the parameter vector \( \hat{\beta} \) fixed at \( \hat{\beta}_1 \), conduct an adaptive search for an improved \( X(\hat{\beta}_1) \). Step 2.B. Compute the estimate \( \hat{\beta}_2 \) for the model based on \( X(\hat{\beta}_1) \) as well as the associated estimate of \( \hat{\beta} \) with score LCV(\( X(\hat{\beta}_1)\),\( \hat{\beta}_2 \)). If this latter score is within a given tolerance of LCV(\( X(\hat{\beta}_1)\),\( \hat{\beta}_1 \)), stop and use \( X(\hat{\beta}_0) \) and \( \hat{\beta}_1 \) as the solution. Otherwise, iterate until LCV(\( X(\hat{\beta}_1)\),\( \hat{\beta}_{i-1} \)) is within that same tolerance of LCV(\( X(\hat{\beta}_{i-1})\),\( \hat{\beta}_i \)) and use \( X(\hat{\beta}_{i-1}) \) and \( \hat{\beta}_i \) as the solution.

Since \( \hat{\beta}_{i+1} \) is held fixed for the multivariate adaptive search at step \( i,A \) for \( i \geq 1 \), the computational effort is comparable to a univariate adaptive search with as many subjects as there are measurements for the multivariate data. A full adaptive search, on the other hand, estimates the parameter vector \( \Theta \)
for every predictor matrix $X$ considered in the search. While the increased search time may be tolerable for simple covariance structures like CS and AR with only two parameters, this will not be the case for more complex structures, like UN with more than a few conditions. Even for simple covariance structures, speed-up will be important in situations with very large numbers of measurements.

### 2.5. Computational support

Results reported in Section 3 were computed using specialized SAS (SAS Institute, Inc., Cary, NC) macros. Parameters were estimated using either the built-in linear mixed modeling procedure PROC MIXED or algorithms constructed within the interactive matrix language procedure PROC IML. These macros are under development to provide general support for exploratory modeling of multivariate outcomes, extending existing support for univariate outcomes.

### 3. Example Analyses

#### 3.1. Example data

Reported analyses use data on medication-taking adherence for HIV positive subjects. These come from the Adherence through Home Education and Nursing Assessment (ATHENA) Project, a clinical trial assessing the impact of a home-based intervention on adherence to antiretroviral medications [9]. The outcome variable $y$ is self-reported adherence, measured by the proportion of prescribed medications taken within three days prior to each of $r=7$ interview dates at 3 month intervals apart. The data consist of $m=784$ outcome measurements for $n=171$ subjects providing at least one outcome measurement. Summary measures for this outcome are reported in Table 1. Mean adherence attains its minimum at baseline ($t=0$) and its maximum at 12 months into the study. Standard deviations vary somewhat with time, suggesting the need to assess the assumption of homogeneous variance. In any case, these values only provide an imprecise depiction of adherence over time since they do not account for the correlation between measurements for the same subject.

### Table 1

<table>
<thead>
<tr>
<th>Months into study</th>
<th>Number of measurements</th>
<th>Mean</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>170</td>
<td>0.87</td>
<td>0.26</td>
</tr>
<tr>
<td>3</td>
<td>135</td>
<td>0.92</td>
<td>0.18</td>
</tr>
<tr>
<td>6</td>
<td>132</td>
<td>0.91</td>
<td>0.20</td>
</tr>
<tr>
<td>9</td>
<td>117</td>
<td>0.90</td>
<td>0.22</td>
</tr>
<tr>
<td>12</td>
<td>113</td>
<td>0.94</td>
<td>0.17</td>
</tr>
<tr>
<td>15</td>
<td>78</td>
<td>0.89</td>
<td>0.25</td>
</tr>
<tr>
<td>18</td>
<td>39</td>
<td>0.89</td>
<td>0.27</td>
</tr>
</tbody>
</table>

#### 3.2. Impact of the number of folds

Table 2 presents results for adaptively selected fractional polynomial models in time (months into the study) for the data of Section 3.1 under a variety of numbers $k$ of folds. A CS random component structure was used with its parameters re-estimated for each fixed component model considered in the search. The same model with two terms, an intercept plus time to the power 0 (and so a step function), is selected for each choice of $k$, so that the results are robust to the choice of $k$. Furthermore, the LCV scores for these selected models are reasonably close in magnitude, with all but one of them within 1% of the best score, and the single exception ($k=5$) within 2%. Hence, any choice of $k$ as long as it is not too small appears to provide reasonable results in general. On the other hand, the scores are not concave in $k$, but can have multiple local maxima. A reasonable strategy for balancing high scores with low values of $k$ is to use the first local maximum in $k$. It seems only necessary to conduct such an assessment for an important initial case and then use the selected value of $k$, 20 in this case, in all subsequent analyses of a data set.

### Table 2

<table>
<thead>
<tr>
<th>Number of folds</th>
<th>Power transforms</th>
<th>LCV score</th>
<th>% decrease from best</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>0</td>
<td>1.12753</td>
<td>1.8%</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>1.14067</td>
<td>0.6%</td>
</tr>
<tr>
<td>15</td>
<td>0</td>
<td>1.14477</td>
<td>0.3%</td>
</tr>
<tr>
<td>20</td>
<td>0</td>
<td>1.14678</td>
<td>0.1%</td>
</tr>
<tr>
<td>25</td>
<td>0</td>
<td>1.14333</td>
<td>0.4%</td>
</tr>
<tr>
<td>30</td>
<td>0</td>
<td>1.14768</td>
<td>0.0%</td>
</tr>
<tr>
<td>35</td>
<td>0</td>
<td>1.14492</td>
<td>0.2%</td>
</tr>
<tr>
<td>40</td>
<td>0</td>
<td>1.14669</td>
<td>0.1%</td>
</tr>
<tr>
<td>45</td>
<td>0</td>
<td>1.14700</td>
<td>0.1%</td>
</tr>
<tr>
<td>50</td>
<td>0</td>
<td>1.14588</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

* All models include an intercept parameter together with the single indicated transform of time (months into the study).

The selected model generates estimates 0.29 and 0.22 of the correlation and standard deviation, respectively. Estimated expected self-reported adherence for this model is plotted in Figure 1, indicating that, after accounting for the correlation between measurements for the same subject, expected adherence increases from a baseline low of 0.86 to a constant level of 0.91 by 3 months into the study. The contraction stopping tolerance parameter $\tau_{CS}$ was set to 0 for the analyses of Table 2. This speeds up processing time, but in general can produce models with negligible terms. That does not happen for this analysis since both model terms are significantly nonzero ($p<0.001$ for the intercept and $p=0.007$ for the transform of time). The recommended setting $\tau_{CS}=0.02$ of [2], however, is too large since then the constant model is selected. Settings up to 0.003 leave the time
transform in the model while settings over 0.004 remove it, suggesting the use of $\tau_{CS}=0.003$ for other analyses of these data. However, a general approach for stopping the contraction is needed.

Stone [10] provides an argument suggesting that differences in $2\log(LCV^m)$ scores for models at consecutive contraction steps would be approximately $\chi^2$ distributed. Since each step produces a model with one less term, the appropriate degrees of freedom df would be 1, but only if the models are nested. This need not necessarily hold since powers are adjusted at each step, but df=1 would be a conservative choice. Hence, a possible way to choose $\tau_{CS}$ would be to test for such a significant difference at $\alpha=0.05$, i.e., a difference exceeding the 95th percentile $3.84146$ of the $\chi^2$ distribution with df=1. Consequently, $\tau_{CS}=1-e^{-1.92073/m}$. For the self-reported adherence data with $m=784$, $\tau_{CS}=0.00245$, so that the time transform appropriately remains in the model. However, since this approach is based on an asymptotic approximation, it requires that m be reasonably large. The value of $\tau_{CS}=0.02$ was recommended in [2] since it proved effective for sample sizes of up to 100. Since $\tau_{CS}>0.02$ if and only if $m \leq 95$, it seems best to leave $\tau_{CS}=0.02$ for $m \leq 95$, and only base $\tau_{CS}$ on the above test for $m > 95$. In any case, this requires further investigation using other data sets.

### 3.3. Alternating component selection

Table 3 presents results for the alternating component selection algorithm of Section 2.4 using 20 folds (as justified in Section 3.2) and the CS covariance structure. Only the correlation is held fixed for the adaptive search conducted at each step 1.A for $i \geq 1$. The standard deviation is re-estimated for each predictor matrix considered in the search, as it would be in univariate normal outcome situations. An initial estimate of the correlation of 0.29222 is generated at step 0 using a constant fixed component with only an intercept. The correlation is held fixed at this value at step 1.A, adaptively selecting a fractional polynomial model in powers of time starting from the constant model. The fixed component with an intercept and the single transform with a power 0 is selected. This is then held constant at step 1.B and the correlation is re-estimated as 0.29397. This latter model is exactly the same model as is selected by the full adaptive search used in Section 3.2, which re-estimates the correlation for each predictor matrix considered in the search. In step 2.A, the correlation is held fixed at 0.29397 while conducting an adaptive search, but starting this time at the step 1 fixed component model. This search leaves the fixed component unchanged, and so step 2.B also leaves the correlation unchanged and the algorithm converges.

#### Table 3

<table>
<thead>
<tr>
<th>Step</th>
<th>Power Transforms</th>
<th>Correlation</th>
<th>LCV Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>--</td>
<td>0.29222</td>
<td>1.14294</td>
</tr>
<tr>
<td>1.A</td>
<td>0</td>
<td>0.29222</td>
<td>1.14955</td>
</tr>
<tr>
<td>1.B</td>
<td>0</td>
<td>0.29397</td>
<td>1.14678</td>
</tr>
<tr>
<td>2.A</td>
<td>0</td>
<td>0.29397</td>
<td>1.14955</td>
</tr>
<tr>
<td>2.B</td>
<td>0</td>
<td>0.29397</td>
<td>1.14678</td>
</tr>
</tbody>
</table>

*a All models include an intercept parameter together with the indicated transform of time (months into the study) if any.

These results indicate that alternating component selection can provide a reasonable alternative model to the one generated through a full adaptive search. It also suggests the possibility that a single step procedure may be effective and that the generated model may even be the same model as is generated by the full adaptive search. Further investigation, though, is needed of this algorithm’s performance with other data sets and other covariance structures, either fixed or selected from among classes of such structures. When assessing results for individual steps, step A scores should not be compared to scores for the other steps since they are inflated due to not considering the effect of estimating the correlation.

### 3.4. Alternative covariance structures

Table 4 presents 20-fold LCV scores for the fixed component selected under the CS covariance structure (i.e., with an intercept and a single power 0 of time), but with alternative covariance structures. The best score is generated using the CS structure, indicating that this structure provides a reasonable description of the covariances for the self-reported adherence data, compared to the other structures considered in Table 4. CS outperforms AR indicating that the correlations are more reasonably considered to be constant over time than to weaken as outcomes become further apart in time. CS also outperforms UN, but distinctly more so. UN generates a 19.1% decrease in LCV score compared to 2.3% for AR, and so there is a distinct penalty to including so many more covariance parameters (21
correlations plus a variance). Heterogeneous variance extensions CSH and ARH do not provide improvements over associated homogeneous variance models CS and AR, indicating that the standard deviations reported in Table 1 do not distinctly vary from a constant value.

**Table 4**

<table>
<thead>
<tr>
<th>Covariance Structure</th>
<th>LCV score</th>
<th>% decrease from best</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS</td>
<td>1.14678</td>
<td>0.0%</td>
</tr>
<tr>
<td>AR</td>
<td>1.12067</td>
<td>2.3%</td>
</tr>
<tr>
<td>UN</td>
<td>0.92793</td>
<td>19.1%</td>
</tr>
<tr>
<td>CSH</td>
<td>1.12695</td>
<td>1.7%</td>
</tr>
<tr>
<td>ARH</td>
<td>1.09660</td>
<td>4.4%</td>
</tr>
</tbody>
</table>

All models include an intercept parameter together with the single power 0 of time (months into the study) as generated under CS.

These results suggest that CS is a reasonable choice for further analyses of these self-reported adherence data. However, this is unlikely to hold in general, and so it is important to have the capability for adaptive fixed component model selection under a variety of covariance structures including those of Table 4, but that is an issue for future research.

4. Conclusion

Adaptive methods for exploratory modeling of repeated measures data based on likelihood cross-validation were formulated and then demonstrated using self-reported adherence over time from a study of HIV positive subjects on antiretroviral therapy. This demonstration primarily addressed the special case of compound symmetry with homogeneous variance, but this covariance structure was shown to be an effective choice for these data. Procedures for choosing the number of cross-validation folds, for speeding up the model selection process, and for stopping that process were also investigated and found effective. Further work is needed to evaluate these methods on a variety of other data sets and to provide general support for exploratory mixed modeling. Future development plans include support for a wider variety of covariance structures as well as for adaptive selection of the covariance structure. For example, the adaptive procedures of Section 2.3 for searching through fractional polynomial models for the expected value can be extended to identify nonparametric heterogeneous variances in terms of nonnegative fractional polynomials. They can be extended as well to identify nonparametric hierarchical linear models based on adaptively selected fractional polynomials with random coefficients.

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