A two-stage estimation procedure for non-linear structural equation models

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SUMMARY

Applications of structural equation models (SEMs) are often restricted to linear associations between variables. Maximum likelihood (ML) estimation in non-linear models may be complex and require numerical integration. Furthermore, ML inference is sensitive to distributional assumptions. In this paper, we introduce a simple two-stage estimation technique for estimation of non-linear associations between latent variables. Here both steps are based on fitting linear SEMs: first a linear model is fitted to data on the latent predictor and terms describing the non-linear effect are predicted by their conditional means. In the second step, the predictions are included in a linear model for the latent outcome variable. We show that this procedure is consistent and identifies its asymptotic distribution. We also illustrate how this framework easily allows the association between latent variables to be modelled using restricted cubic splines and we develop a modified estimator which is robust to non-normality of the latent predictor. In a simulation study, we compare the proposed method to MLE and alternative two-stage estimation techniques.
1 Introduction

Over the last decades linear structural equation models have been useful in many fields of research. These models typically consists of two parts, a measurement part where observed outcomes are assumed to be reflections of underlying latent variables and a structural part relating the latent variables to each other. Important extensions of this framework have used more flexible measurement models to allow inclusion of binary, ordinal and censored outcomes (Muthén (1984), Skrondal and Rabe-Hesketh (2004)). In this paper we focus on the structural part and consider models which allow for non-linear relations between the latent variables. Until now most research in this topic has been on the interaction model assuming a linear effect of the product of two latent variables (i.e., \( \eta = \beta_1 \xi_1 + \beta_2 \xi_2 + \beta_3 \xi_1 \xi_2 + \zeta \)) or more general polynomial models including terms of higher order (e.g., \( \eta = \beta_1 \xi_1 + \beta_2 \xi_1^2 + \zeta \)), but a more general framework is of obvious interest.

Maximum likelihood inference in linear SEMs are facilitated by the fact that a closed form expression for the likelihood function is obtained when integrating out the latent variables. Non-linear models do not have this property and numerical methods are needed. Today, the so-called LMS algorithm (Klein and Moosbrugger, 2000) is perhaps the most widely used method. It approximates the likelihood function using a mixture of multivariate normal distributions and then this function is maximized with the EM-algorithm. For simple non-linear models (product-interaction model and second degree polynomial), this algorithm has been implemented in the widely used software package Mplus (Muthén and Muthén, 2012).

An alternative EM-algorithm was proposed by Lee and Zhu (2002), while Wall (2009) used Adaptive Gaussian Quadrature (AGQ) and Rizopoulos and Moustaki (2008) suggested a hybrid EM-algorithm based on AGQ. Bayesian techniques have also been considered for non-linear models (Arminger and Muthén (1998), Lee and Zhu (2000)) and these have been extended to more flexible semi-parametric models (Yang and Dunson (2010), Song et al. (2010), Kelava and Brandt (2014)).

Due to the complexity of the ML-procedure for estimation of non-linear SEMs, a number of simpler so-called limited information methods have been developed. Kenny and Judd (1984) developed the first estimator for the product-interaction
model by fitting a modified linear model including an additional latent variable with indicators given by products of indicators of the two interacting latent variables. Since then this technique has been refined by several researchers (see Marsh et al. (2004) for an overview), but it remains rather ad-hoc and cannot be used for more general non-linear models. For the polynomial model, Wall and Amemiya (2000) proposed a two-step method (2SMM), where the latent variables were first predicted using the so-called Bartlett score, while the second step estimated the parameters of the non-linear relations using a method-of-moments procedure allowing for uncertainty in the predicted variables. Despite some nice statistical properties, this method has not been used much in practice. Mooijaart and Bentler (2010) developed a method-of-moments procedure by including third degree moments for estimation of non-linear effects in the polynomial model. A computationally very simple two-stage least squares (2SLS) method was developed by Bollen (Bollen (1995), Bollen and Paxton (1998)). Here instrumental variables must be identified also for non-linear terms. It is not clear whether this method can be used in general models, but the method is non-iterative and easy to implement in standard statistical software. However, simulation studies have indicated that this method has a rather low efficiency compared to ML-estimation (Schermelleh-Engel et al., 1998).

In this paper we present a new two-stage method for estimation in non-linear structural equation models. As in 2SMM, we first have a prediction step, but instead of the Bartlett score we use the Empirical Bayes method and instead of predicting the latent variables we predict the latent non-linear effect terms. Therefore, in the second step, it is sufficient to fit a linear structural equation model with the predicted variables included as covariates. We show that the method yields consistent estimation and derive expressions for asymptotic standard errors. We illustrate how splines can be included and by using mixture models in the first step, we extent the method so that it becomes robust to non-normality of latent predictor variables. In simulation studies the method is compared to ML, 2SMM, 2SLS and an alternative two-stage estimator of semi-parametric associations between latent variables (Kelava et al., 2017). Finally, we illustrate the usefulness of the method analysing data from neuroscience on the regional binding potential of different serotonergic markers in the human brain.
2 A non-linear structural equation model

We consider a model where a latent response variable $\eta_i = (\eta_{i1}, \ldots, \eta_{ip})^t$ of subject $i$ ($i = 1, \ldots, n$) is assumed to be non-linearly related to a latent predictor $\xi_i = (\xi_{i1}, ..., \xi_{iq})^t$ after adjustment for covariates $Z_i = (Z_{i1}, ..., Z_{ir})$

$$\eta_i = \alpha + B\varphi(\xi_i) + \Gamma Z_i + \zeta_i,$$  \hspace{1cm} (1)

such that $\varphi(\xi_i) = (\varphi_1(\xi_i), ..., \varphi_l(\xi_i))^t$ has finite variance. The main parameter $B(p \times l)$ describes the non-linear relation between $\xi_i$ and $\eta_i$. Note, that $\varphi$ may also depend on some of the covariates thereby allowing the introduction of interaction terms, but we here omit this to simplify notation.

The latent predictors $(\xi_i)$ are related to each other and the covariates in a linear structural equation

$$\xi_i = \tilde{\alpha} + \tilde{B}\xi_i + \tilde{\Gamma} Z_i + \tilde{\zeta}_i,$$  \hspace{1cm} (2)

where diagonal elements in $\tilde{B}$ are zero and the residual terms $\zeta_i$ and $\tilde{\zeta}_i$ are assumed to be independent with mean 0 and covariance matrices of $\Psi$ and $\tilde{\Psi}$, respectively.

The observed variables $X_i = (X_{i1}, ..., X_{ih})^t$ and $Y_i = (Y_{i1}, ..., Y_{im})^t$ are linked to the latent variable in the two measurement models

$$Y_i = \nu + \Lambda \eta_i + K Z_i + \epsilon_i,$$  \hspace{1cm} \hspace{1cm} (3)

$$X_i = \tilde{\nu} + \tilde{\Lambda} \xi_i + \tilde{K} Z_i + \tilde{\epsilon}_i.$$  \hspace{1cm} (4)

where the error terms $\epsilon_i$ and $\tilde{\epsilon}_i$ are assumed to be independent with mean 0 and covariance matrices of $\Omega$ and $\tilde{\Omega}$, respectively. The parameters are collected into $\theta = (\theta_1, \theta_2)$, where $\theta_1 = (\alpha, \tilde{\alpha}, \beta, \tilde{\beta}, \nu, \tilde{\nu}, \Lambda, \tilde{\Lambda}, K, \tilde{K}, \Psi)$ are the parameters of the linear SEM describing the conditional distribution of $X_i$ given $Z_i$. The rest of the parameters are collected into $\theta_2$.

For identification of the model, we need to impose some parameter constraints (Bollen, 1989). Generally, measurement models can be made identifiable by selecting a reference indicator for each latent variable. For this variable we fix the regression coefficient of the latent variable (element of $\Lambda$ or $\tilde{\Lambda}$) to 1 and the inter-
cept (element of $\nu$ or $\nu$) to 0. Alternatively, the variance of latent variables can be fixed to 1, and their intercepts (element of $\alpha$ or $\alpha$) set to 0. In the estimation procedure described below, it turns out to be crucial to use the reference indicator restriction in the measurement model for $Y_i$. Also, we model the covariance $\Psi$ of the latent outcomes ($\eta_i$) using an unrestricted covariance matrix.

Figure 1: Path diagram showing an example of the non-linear structural equation models considered. The two-stage estimator is constructed by separately estimating parameters of Model 1, and (non-linear) associations between the two models are then estimated in a subsequent step based on predictions from the Model 1 analysis.

The likelihood function is $L(Y, X, Z, \theta) = \prod_{i=1}^{n} p_{\theta}(Y_i, X_i|\eta_i, \xi_i, Z_i)p_{\theta_2}(\eta_i|\xi_i, Z_i)p_{\theta_1}(\xi_i|Z_i)d\xi_id\eta_i$. Assuming joint normality of $(\zeta_i, \tilde{\zeta}_i, \epsilon_i, \tilde{\epsilon}_i)'$, a closed form expression for $L_i$ is available only if $\phi$ is linear. In the general case numerical integration techniques are necessary for ML-estimation, which in practice for even moderately sized problems (number of latent variables) is computationally intractable. Instead, we exploit that the structural equation (1) is linear in the parameters to get

$$E(\eta_i|X_i, Z_i) = \alpha + B\mathbb{E}_{\theta_1}[\phi(\xi_i)|X_i, Z_i] + \Gamma Z_i,$$

noting that the conditional expectation on the right-hand side depends only on the distribution parametrized by $\theta_1$. Equation (5) suggests that parameters can
be estimated in two steps. First, the linear SEM given by equations (2) and (4) is fitted to \((X_i, Z_i, i = 1, \ldots, n)\) and the latent covariate \(\varphi(\xi_i)\) is predicted by the conditional mean \(E_{\hat{\theta}_1}[\varphi(\xi_i)|X_i, Z_i]\). Step 2 then estimates \(\theta_2\) in a linear SEM, where the measurement model is given by equation (3) and the structural model is equation (1) with the latent predictor replaced by \(E_{\hat{\theta}_1}[\varphi(\xi_i)|X_i, Z_i]\). Thus, the key idea is to replace \(\varphi(\xi_i)\) by (an estimate of) the conditional mean of \(\varphi(\xi_i)\) given \(X\) and \(Z\). Previous methods have used \(\varphi\) of the conditional mean \(E_{\hat{\theta}_1}[\xi_i|X_i, Z_i]\) (Jöreskog and Yang (2000), Schumacker (2002)).

In the following we will use the notation \(\varphi^*_i(\xi_i) = E[\varphi(\xi_i) | X_i, Z_i]\) and \(\varphi^*_n(\xi_i) = E_{\hat{\theta}_1}[\varphi(\xi_i) | X_i, Z_i]\) to distinguish between the conditional expectation and the plug-in estimator, where the expectation is taken with respect to the distribution indexed by the estimated parameter values from the stage one model. To summarize, we define the two-stage estimator in the following way

**Remark 1** (Two-Stage Structural Equation Model estimator \((2SSEM)\)).

1. The linear SEM given by equations (2) and (4) is fitted to \((X_i, Z_i, i = 1, \ldots, n)\) to achieve an estimate of the parameter \(\theta_1\).

2. The parameter \(\theta_2\) is estimated via a linear SEM with measurement model given by equation (3) and structural model given by equation (1), where the latent predictor, \(\varphi(\xi_i)\), is replaced by \(\varphi^*_n(\xi_i)\).

We can now formulate the consistency properties of the proposed estimator (the asymptotic distribution of \(2SSEM\) is derived in Section 4).

**Theorem 1.** Under a correctly specified non-linear SEM (1)-(4) including correctly specified distribution of the residual terms, \(2SSEM\) will yield consistent estimates of all parameters \((\theta)\) except for the residual covariance, \(\Psi\), of the latent variables in step 2.

**Proof.** Since the exposure part of the model is correctly specified, \(\theta_1\) is estimated using ML-estimation and therefore \(\hat{\theta}_1\) is consistent under mild regularity conditions (Anderson and Amemiya, 1988). In step two, the model is misspecified as we fit a linear model to a non-linear association. We prove the theorem by showing
that even though the model is misspecified it includes the true mean and covariance of the data. When fitting a linear SEM with correctly specified mean and variance, the estimator \( \hat{\theta}_2 \) will converge to the parameter value which induces the true mean and variance (Arminger and Schoenberg, 1989). Finally, we characterize this parameter value and see that it is identical to the truth \( (\theta_2) \) except for elements describing the residual covariance of the latent variables in step 2 (\( \Psi \)). We make these arguments assuming that the predicted values \( \varphi^* \) were available.

The result then follows from the Continuous Mapping Theorem and by noting that \( \varphi^*_n \to \varphi^* \) a.s. as \( n \to \infty \). The proof is illustrated in the situation where \( K = 0 \), as this simplifies matrix expressions without affecting theoretical insights (see the appendix for a more general formulation).

The next step is to show that the model fitted in step-two induces the correct mean and variance structure for the data \( V_i = (Z^*_i, \varphi^*(\xi)^t, Y^+_i)^t \). To save space, we illustrate this only for the variance (full proof is given in appendix). In step two, we fit a linear model with correct measurement part \( Y_i = \nu_2 + \Lambda_2 \eta_i + \epsilon_i \) and structural part \( \eta_i = \alpha_2 + B_2 \varphi^*(\xi_i) + \Gamma_2 Z_i + \zeta_i \). Here the subscript 2 is used to distinguish the parameters of step-two model from the true parameter value (no subscript). Using standard results from linear models (Bollen, 1989), and the notation \( \Sigma_{z,\varphi} = \Sigma_{\varphi,z} \), the modelled variance is

\[
\Sigma_{V_i} = \begin{pmatrix}
\Sigma_Z & \Sigma_{z,\varphi} \\
0 & \Sigma_{\varphi} & [\Sigma_{\varphi} B_2^t + \Sigma_{\varphi,z} \Gamma_2^t] \Lambda_2^t \\
0 & 0 & \Lambda_2 \Sigma_{\eta} \Lambda_2^t + \Omega_2
\end{pmatrix}
\]

(6)

where \( \Sigma_{\eta} = B_2 \Sigma_{\varphi} B_2^t + B_2 \Sigma_{\varphi,z} \Gamma_2^t + \Gamma_2 \Sigma_{\varphi,z} B_2^t + \Gamma_2 \Sigma_Z \Gamma_2^t + \Psi_2 \) is the modelled variance of \( \eta \) and \( \Sigma_Z, \Sigma_{z,\varphi}, \Sigma_{\varphi} \) are completely unstructured parameters modelling the variance of the step-two covariates \( (Z_i, \varphi^*(\xi_i)) \). To calculate the true variance, we write the structural model as

\[
\eta_i = \alpha + B \varphi(\xi_i) + \Gamma Z_i + \zeta_i = \alpha + B \varphi^*(\xi_i) + B[\varphi(\xi_i) - \varphi^*(\xi_i)] + \Gamma Z_i + \zeta_i
\]

(7)
and from this we derive the variance of the latent variable $\eta_i$

$$\text{Var}(\eta_i) = B \text{Var}[\varphi^*(\xi_i)] B^t + B \text{Cov}[\varphi^*(\xi_i), Z_i] \Gamma^t + \Gamma \text{Cov}[Z_i, \varphi^*(\xi_i)] B^t + B \text{Var}[\varphi(\xi_i) - \varphi^*(\xi_i)] B^t + \Gamma \text{Var}(Z) \Gamma^t + \Psi,$$  

(8)

because $\text{Cov}[\varphi^*(\xi_i), \varphi(\xi_i) - \varphi^*(\xi_i)] = 0$ and $\text{Cov}[Z_i, \varphi(\xi_i) - \varphi^*(\xi_i)] = 0$, which follows from the law of iterated expectations. We can now determine the co-variances $\text{Cov}[\varphi^*(\xi_i), Y_i] = \text{Cov}[\varphi^*(\xi_i), \Lambda \eta_i] = \text{Cov}[\varphi^*(\xi_i), B \varphi^*(\xi_i) + \Gamma Z_i] \Lambda^t + \text{Cov}[\varphi^*(\xi_i), \varphi(\xi_i) - \varphi^*(\xi_i)] = 0$ and $\text{Cov}(Z_i, Y_i) = \text{Cov}(Z_i, \Lambda \eta_i) = \text{Cov}(Z_i, B \varphi^*(\xi_i) + \Gamma Z_i) \Lambda^t$ as $\text{Cov}[Z_i, \varphi(\xi_i) - \varphi^*(\xi_i)] = 0$. Finally, the variance is

$$\text{Var}(V_i) = \begin{pmatrix}
\text{Var}(Z_i) & \text{Cov}[Z_i, \varphi^*(\xi_i)] & \text{Var}[\varphi^*(\xi_i)] B^t + \text{Cov}[Z_i, \varphi^*(\xi_i)] \Gamma^t \Lambda^t \\
. & \text{Var}[\varphi^*(\xi_i)] & \text{Var}[\varphi^*(\xi_i)] B^t + \text{Cov}[\varphi^*(\xi_i), Z_i] \Gamma^t \Lambda^t \\
. & . & \Lambda \text{Var}(\eta_i) \Lambda^t + \Omega
\end{pmatrix}.$$  

(9)

It can now be seen that the modelled variance is equal to the true variance [(6) = (9)] and the modelled mean is equal to the true mean (equations not shown) if $B_2 = B, \Lambda_2 = \Lambda, \Gamma_2 = \Gamma, \Omega_2 = \Omega, \alpha_2 = \alpha, \nu_2 = \nu, \mu_\varphi = \mathbb{E}[\varphi(\xi_i)], \mu_Z = \mathbb{E}(Z_i), \Sigma_{Z,\varphi} = \text{Cov}(Z_i, \varphi^*(\xi_i)), \Sigma_\varphi = \text{Var}[\varphi^*(\xi_i)], \Sigma_Z = \text{Var}(Z_i)$ and $\Psi_2 = \Psi + B \text{Var}[\varphi(\xi_i) - \varphi^*(\xi_i)] B^t$. Note, that although the expression for the modelled variance of the latent variable ($\Sigma_{\eta_i}$) is missing the term $B \text{Var}[\varphi(\xi_i) - \varphi^*(\xi_i)] B^t$, the model can achieve the correct variance for $Y_i$ by adding the missing term to the residual variance $\Psi_2$. Since the model includes the true mean and variance, $\hat{\theta}_2$ will converge to the specific parameter value inducing this mean and variance. Therefore, all parameters are consistently estimated except for the variance of the latent variable, which will be overestimated. \hfill \Box

An important advantage of the proposed method is that closed form expressions for $\varphi^*(\xi_i)$ are available for large classes of functions including polynomials and splines basis functions (see Section 3) making the implementation of the estimator straightforward and computationally fast. Also, note that the formulation of Theorem 1 is overly restrictive, as it states that consistency relies not only on a correctly specified model structure, but also on correctly specified distributions of residuals. However, linear SEMs only require a correctly specified mean and variance (conditional on covariates) to yield consistent estimation (Arminger and Schoenberg,
989) and therefore 2SSEM will be robust to distributional misspecifications. Thus, non-normality of the residuals of the measurement models in step two will not affect consistency. However, for $\hat{\theta}_2$ to be consistent, we note that the following conditions must hold: (a) $\mathbb{E}[\varphi(\xi_i) - \varphi^*(\xi_i)] = 0$, (b) $\text{Cov}[\varphi^*(\xi_i), \varphi(\xi_i) - \varphi^*(\xi_i)] = 0$, (c) $\text{Cov}[Z_i, \varphi(\xi_i) - \varphi^*(\xi_i)] = 0$. These are obviously fulfilled when the conditional mean $\mathbb{E}[\varphi(\xi_i) \mid X_i, Z_i]$ is correctly modelled. To address this both the stage 1 and stage 2 model fits should be assessed using standard model checking tools for linear SEMs (Sánchez et al., 2009b). Here the critical distribution is that for the residual $\tilde{\zeta}_i$ of the latent exposure, whereas correct specification of error terms in the measurement model of the stage one model is less important as shown in simulations of Section 5. In Section 2.1, we describe an extended method which allow flexible models for the distribution of the latent exposure variable.

A few consequences of the calculations in the proof of Theorem 1 are important to note. Firstly, it is important that the step-two model uses an unstructured covariance matrix ($\Psi_2$) for the variance of the latent variable. If that is not the case, it may be impossible for the model to account for the misspecification of $\Sigma_\eta$ ($\Sigma_\eta \neq \text{Var}(\eta_i)$), therefore the modelled variance of $V_i = (Z_i^t, \varphi^*(\xi_i)^t, Y_i^t)^t$ may be wrong and estimation will likely become inconsistent. In particular, the model should not be made identifiable by fixing the variance of the latent variable to one. Secondly, covariates that are used in the step-two model, must also be present in the first step. If that is not the case, $\text{Cov}[Z_i, \varphi(\xi_i) - \varphi^*(\xi_i)]$ may not be zero and the step-two model will have an incorrect variance leading to inconsistent estimation. Thirdly, in the step-two model, the covariance terms $\text{Cov}[Z, \varphi^*(\xi_i)]$ and $\text{Var}[\varphi^*(\xi_i)]$ are modelled using unstructured matrices so that any information these terms might have had about the parameters is disregarded in this approach. Finally, note that in Theorem 1 it is assumed that variables in the stage one model affects the variables in the stage two model only indirectly through the latent variable. In the presence of a direct effect from one of the indicators, $X_i$, either on the latent variable or the indicators of the stage two model, the proposed method can easily be extended by simply including the relevant indicators as covariates in the stage two model. The consistency of this approach is proven in Appendix A.

It is interesting to compare our method to the two-stage method-of-moments (2SMM) of Wall and Amemiya (2000). Here predictions $\hat{\xi}$ and $\hat{\eta}$ of the latent
variables are calculated from a confirmatory factor analysis model and then the second step fits a non-linear regression model \( \hat{\eta} = \beta \varphi(\hat{\xi}) + \zeta \) allowing for uncertainty in \( \hat{\xi} \). For the latter task a method moments estimator is used, but it works only for polynomial models. Our method is different from 2SMM in two important ways. Rather than predicting \( \xi \) in step one, we predict the non-linear terms \( \varphi(\xi) \) and therefore we are left with a linear model in step two. Of course the predicted terms are different from the latent true terms, so, as in 2SMM, we have measurement error in covariates in the second step. Here the choice of prediction method in step one becomes important. We use the conditional mean \( \varphi^*(\xi_i) = \mathbb{E}[\varphi(\xi)|X, Z] \) which has Berkson errors, that is the prediction in uncorrelated with the prediction error \( \text{Cov}[\varphi^*(\xi_i), \varphi(\xi_i) - \varphi^*(\xi_i)] = 0 \). In linear regression models, it is well-known that Berkson errors will not bias regression coefficients (Carroll et al., 2006). In step two we estimate parameters using a linear model and therefore the Berkson errors do not lead to inconsistency as we show in Theorem 1. In contrast, Bartlett predictions (used in 2SMM) have classic error and therefore adjustments are needed in order to achieve unbiased estimation.

### 2.1 Extension to mixtures of structural equation models

In this section we extend the structural part of the model to allow for non-normal latent predictor variables. This is done through a mixture model. Thus, let \( G_i \sim \text{multinom}(\pi) \) be the class indicator \( G_i \in \{1, \ldots, K\} \), and \( \xi_i \) the \( q \)-dimensional latent predictor \( \xi_i = \sum_{k=1}^{K} I(G_i = k) \xi_{ki} \), where each component \( \xi_{ki} \) follows a linear structural equation

\[
\xi_{ki} = \tilde{\alpha}_k + \tilde{B}\xi_{ki} + \tilde{\Gamma}Z_i + \tilde{\zeta}_{ki},
\]

with \( \tilde{\zeta}_{ki} \sim N(0, \tilde{\Psi}_k) \). We assume \( G_i \) to be independent of \( (\tilde{\zeta}_{1i}, \ldots, \tilde{\zeta}_{Ki}) \) and \( (\epsilon_i, \tilde{\epsilon}_i) \). Results can be extended also to the case where \( \pi \) depends on covariates. Note, that the extension concerns only the conditional distribution of the latent predictor given the covariates. Thus, the only parameters that depend on \( k \) is the intercept and the variance in the structural model for \( \xi \), whereas the measurement models and the structural model for \( \eta_i \) remain as shown in equations (1, 3, 4) independent of \( k \).
In the extended model, the two-step procedure is modified by the fact that ML-estimation in step 1 will be more complex (typically done via the EM algorithm) and the predicted latent variables now become

\[ E[\varphi(\xi_i)|X_i, Z_i] = E\{E[\varphi(\xi_i)|X_i, Z_i, G_i]|X_i, Z_i\} \]

\[ = \sum_{k=1}^{K} P(G_i = k|X_i, Z_i) E[\varphi(\xi_{ki})|X_i, Z_i, G_i = k] \]  

\[ = \sum_{k=1}^{K} P(G_i = k|X_i, Z_i) E[\varphi(\xi_{ki})|X_i, Z_i], \]  

(11)

where the last step uses the fact that \( G_i \) is independent of \((\zeta_{ki}, \tilde{\epsilon}_i)\). So the predictions of step 1 are the sum of the product of the posterior probabilities (class probabilities which are by-products of the EM algorithm) and predictions of the type described in Section 3. Of course, the second step in the estimation procedure is unchanged: a linear SEM is fitted with the predictions included as covariates.

### 3 Prediction of non-linear latent terms

In this section, we show that for important classes of non-linear functions \((\varphi)\) closed form expressions can be derived for \( \varphi^*(\xi_i) = E[\varphi(\xi_i)|X_i, Z_i] \). Under the assumptions of the model, the conditional distribution of \( \xi_i \) given \( X_i \) and \( Z_i \) is normal with mean and variance

\[ m_{x,z} = \mathbb{E}(\xi_i|X_i, Z_i) = \tilde{\alpha} + \tilde{\Gamma}Z_i + \Sigma_{X\xi}\Sigma_{X}^{-1}(X_i - \mu_X) \]

\[ \nu = \text{Var}(\xi_i|X_i, Z_i) = \tilde{\Psi} - \Sigma_{X\xi}\Sigma_{X}^{-1}\Sigma_{X}, \]  

(12)

where \( \mu_X = \tilde{\nu} + \tilde{\Lambda}(I - \tilde{B})^{-1}\alpha + \tilde{\Lambda}(I - \tilde{B})^{-1}\tilde{\Gamma}Z_i + KZ_i, \Sigma_X = \tilde{\Lambda}(I - \tilde{B})^{-1}\tilde{\Psi}(I - \tilde{B})^{-1}\tilde{\Lambda} + \tilde{\Omega} \) and \( \Sigma_{X\xi} = \tilde{\Lambda}(I - \tilde{B})^{-1}\tilde{\Psi}(I - \tilde{B})^{-1}\tilde{\Lambda} \). Note that the conditional variance does not depend on \( X \) and \( Z \). Below we will consider a number of non-linear models and provide expressions for \( E[\varphi(\xi_i)|X_i, Z_i] \). In addition, we will briefly compare our method to regression calibration (Carroll et al., 2006), where the second stage model simply would use \( \varphi(m_{x,z}) \) as a covariate in a linear SEM.

We start by considering univariate functions, so we assume \( \xi_i \) to be a scalar.

**Example 1. Polynomials**

\[ \eta_i = \alpha + \sum_{m=1}^{k} \beta_m \xi_i^m + \zeta_i, \]  

(13)
Here \( \varphi(\xi_i) = \xi_i^m \) \((m \in \mathbb{N})\) and conditional means are given by
\[
\mathbb{E}(\xi_i^m|X_i, Z_i) = \sum_{k=0}^{[m/2]} m_{x,z}^{m-2k} v^k \frac{m!}{2^k k!(m-2k)!} \tag{14}
\]
In the quadratic model \((\eta_i = \alpha + \beta_1 \xi_i + \beta_2 \xi_i^2 + \zeta_i)\), \(\mathbb{E}(\xi_i^2|X_i, Z_i) = m_{x,z}^2 + v\) and therefore \(\mathbb{E}(\eta_i|X_i, Z_i) = \alpha + \beta_1 m_{x,z} + \beta_2 m_{x,z}^2 + \beta_2 v\). So in this model, regression calibration uses a correct expression for the mean of \(\eta_i\) except that the term depending on \(v\) will not be included and therefore the intercept will be estimated with bias. However, in a third-degree model, \(\mathbb{E}(\xi_i^3|X_i, Z_i) = m_{x,z}^3 + 3m_{x,y}v\) and the regression calibration approach of just replacing \(\xi_i\) with \(m_{x,z}\) will lead to biased coefficients of the polynomial.

**Example 2.** For the exponential function \(\varphi(\xi_i) = \exp(\xi_i)\) an expression can be obtained as \(\exp(\xi_i)\) will follow a logarithmic normal distribution where the mean is
\[
\mathbb{E}[\exp(\xi_i)|X_i, Z_i] = \exp(0.5v + m_{x,y}) \tag{15}
\]
Again, regression calibration is biased as the outcome is regressed on \(\exp(m_{x,y})\) and not \(\exp(0.5v + m_{x,y})\). If the conditional variance \((v)\) is small then the bias is expected also to be small. The conditional mean of functions on the form \(\varphi(\xi_i) = \exp(\xi_i)^m\) is straightforward to calculate as this variable again follows a logarithmic normal distribution.

**Example 3.** A piece-wise linear relation is described by
\[
\eta_i = \alpha + \beta_1 (\xi_i 1_{\{\xi_i < \tau\}} + \tau 1_{\{\xi_i > \tau\}}) + \beta_2 (\xi_i - \tau) 1_{\{\xi_i > \tau\}} + \zeta_i, \tag{16}
\]
where \(\tau\) is a known break-point. As illustrated in Appendix ?? closed form expressions for the predictions can be calculated, i.e.,
\[
\begin{align*}
\mathbb{E}(\xi_i 1_{\{\xi_i < \tau\}}|X_i, Z_i) &= m_{x,z} \Phi\left(\frac{\tau - m_{x,z}}{s}\right) - s \Phi\left(\frac{\tau - m_{x,z}}{s}\right) \\
\mathbb{E}((\xi_i - \tau) 1_{\{\xi_i > \tau\}}|X_i, Z_i) &= (m_{x,z} - \tau)[1 - \Phi\left(\frac{\tau - m_{x,z}}{s}\right)] + s \Phi\left(\frac{\tau - m_{x,z}}{s}\right),
\end{align*} \tag{17}
\]
where \( \phi \) and \( \Phi \) are the density function and the cumulative distribution function of the standard normal distribution and \( s = \sqrt{v} \). Clearly, regression calibration will generally provide inconsistent estimates in this model.

**Example 4.** A natural cubic spline with \( k \) knots \( t_1 < t_2 < \ldots < t_k \) is given by

\[
\eta_i = \alpha + \beta_0 \xi_i + \sum_{j=1}^{k-2} \beta_j f_j(\xi_i) + \zeta_i, \tag{18}
\]

with \( f_j(\xi_i) = g_j(\xi_i) - \frac{t_k-t_j}{t_k-t_{k-1}} g_{k-1}(\xi_i) + \frac{t_{k-1}-t_j}{t_{k-1}-t_{k-2}} g_k(\xi_i), \) \( j = 1, \ldots, k-2 \) and \( g_j(\xi_i) = (\xi_i - t_j)^31_{\xi_i > t_j}, \) \( j = 1, \ldots, k \) (Durrleman and Simon, 1989). Thus, predictions \( E[f_j(\xi_i)|X_i, Z_i] \) are linear functions of \( E[g_j(\xi_i)|X_i, Z_i] \). In the Appendix we derive the following expressions for these means, i.e.,

\[
E[g_j(\xi_i)|X_i, Z_i] = \frac{s}{\sqrt{2\pi}}[(2s^2 + (m_{x,z} - t_j)^2) \exp(-\frac{(m_{x,z} - t_j)^2}{2s^2}) + (m_{x,z} - t_j)[(m_{x,z} - t_j)^2 + 3s^2]p_{x,z,j}], \tag{19}
\]

where \( s = \sqrt{v} \) and \( p_{x,z,j} = P(\xi_i > t_j|X_i, Z_i) = 1 - \Phi(\frac{t_j - m_{x,z}}{s}) \). Also, in this model, regression calibration will generally provide inconsistent estimates.

The previous examples have focused on regression equations with only one latent predictor. Of course these calculations can easily be extended to models with multiple predictors with non-linear effects as long as the terms enter the model additively. Non-linear terms depending on multiple latent variables are more complex. The last example describes the most common non-linear function involving two variables where interactions are modelled using product terms.

**Example 5.** Product-interaction model

\[
\eta_i = \alpha + \beta_1 \xi_{1i} + \beta_2 \xi_{2i} + \beta_{12} \xi_{1i} \xi_{2i} + \zeta_i, \tag{20}
\]

Now \( E(\xi_{1i}\xi_{2i}|X_i, Z_i) = \text{Cov}(\xi_{1i}, \xi_{2i}|X_i, Z_i) + E(\xi_{1i}|X_i, Z_i)E(\xi_{2i}|X_i, Z_i) \), where terms on the right-hand side are directly available from the bivariate normal distribution of \( \xi_{1i}, \xi_{2i} \) given \( X_i, Z_i \). Regression calibration leads to the correct mean expect that the intercept will be biased as this method will not include the covariance term above.
4 Asymptotic properties of the two-stage estimator

From Theorem 1 we have consistency of all structural parameters in the stage 2 model. In this section, we show that the limiting distribution of the estimator is asymptotically normal, and we derive the asymptotic variance via the estimated influence functions of the stage 1 and stage 2 estimators.

In the following we assume that the observations \((Y_i, X_i, Z_i), i = 1, \ldots, n\) are i.i.d., and we also restrict attention only to the consistent estimates as mentioned in the previous section, i.e., \(\theta_2\) does not contain any of the parameters belonging to \(\Psi\).

We will assume that the stage 1 model estimator is obtained as the solution to the following score equation:

\[
U_1(\theta_1; X, Z) = \sum_{i=1}^{n} U_1(\theta_1; X_i, Z_i) = 0,
\]

which typically will be the score of the usual Maximum Likelihood Estimator. Similarly, if we could observe the latent variables in the stage 1 model, a consistent estimator of the stage 2 model would be obtained by solving a score equation corresponding to another linear SEM

\[
U_2(\theta_2; Y, X, Z, \xi) = \sum_{i=1}^{n} U_2 (\theta_2; Y_i, Z_i, \phi(\xi_i)) = 0.
\]

As shown in Theorem 1, a consistent estimator for \(\theta_2\) can be obtained by instead considering the score equation

\[
U_2(\theta_2; Y, X, Z) = \sum_{i=1}^{n} U_2 (\theta_2; Y_i, Z_i, \phi^*(X_i, Z_i)) = 0,
\]

where \(\phi^*(X_i, Z_i) = \mathbb{E}_{\theta_{01}}(\phi(\xi_i) \mid X_i, Z_i)\). Denote the simultaneous score function

\[
U(\theta_2, \theta_1; Y, X, Z) = \sum_{i=1}^{n} U_2 \left(\theta_2, Y_i, Z_i, \widehat{\phi^*}(X_i, Z_i; \theta_1)\right),
\]

where we have plugged in the predictions from the first model \(\widehat{\phi^*}(X_i, Z_i; \theta_1) = \mathbb{E}_{\theta_{01}}(\phi(\xi_i) \mid X_i, Z_i)\).
\( \mathbb{E}_{\theta_1}(\varphi(\xi_i) \mid X_i, Z_i) \) evaluated at the parameter \( \theta_1 \).

Let in the following \( \nabla_{\theta} \mathcal{U}(\theta) \) denote the \( m \times m \) matrix of partial derivatives of \( \mathcal{U} \), where \( m \) is the dimension of the joint parameter vector \( \theta \). We will impose the following regularity conditions in addition to the consistency assumptions in Theorem 1:

(a) The estimator of the stage 1 model is consistent, linear, regular, and asymptotic normal.

(b) \( \mathcal{U} \) is twice continuous differentiable in a neighbourhood around the true (limiting) parameters \((\theta_{01}^{T}, \theta_{02}^{T})^{T}\). Further,

\[
\frac{1}{n} \sum_{i=1}^{n} n^{-1} \nabla U_2(Y_i, X_i, Z_i; \theta_1, \theta_2)
\]

converges uniformly to \( \mathbb{E}[\nabla U_2(Y_i, X_i, Z_i; \theta_1, \theta_2)] \) in a neighbourhood around \((\theta_{01}^{T}, \theta_{02}^{T})^{T}\),

(c) and when evaluated here \(-\mathbb{E}(\nabla U_2)\) is positive definite.

We first note that assumption (a) means that

\[
\sqrt{n}(\hat{\theta}_1 - \theta_{01}) = \frac{1}{\sqrt{n}} \sum_{i=1}^{n} IF_1(X_i, Z_i; \theta_{01}) + o_p(1),
\]

where \( IF_1 \) is the influence function of the estimator (Stefanski and Boos, 2002). Similarly, (23) defines a regular consistent \( m \)-estimator, and for known \( \theta_{01} \), it follows along the lines of (Newey and McFadden, 1994, Theorem 3.4), (Tsiatis, 2006, Chapter 3) from assumptions (b)-(c) that

\[
\sqrt{n}(\hat{\theta}_2(\theta_{01}) - \theta_{02}) = \frac{1}{\sqrt{n}} \sum_{i=1}^{n} IF_2(Y_i, Z_i, \varphi^*(X_i, Z_i); \theta_{02}) + o_p(1),
\]

where the influence function is given by

\[
IF_2(Y_i, Z_i, \varphi^*(X_i, Z_i); \theta_{02}) = \mathbb{E} ((-\nabla_{\varphi^*} U_2(Y, Z, \varphi^*(X, Z), \theta_{02})) U_2(Y_i, Z_i, \varphi^*(X_i, Z_i), \theta_{02})).
\]  

(24)
A sufficient criterion for the uniform convergence is that the covariates are all bounded.

Denote $\hat{\theta}_2(\theta_1)$ as the estimator obtained from solving (23) with fixed stage 1 parameter at $\hat{\theta}_1$. A Taylor expansion around $\theta_{01}$ (see (Newey and McFadden, 1994, Chapter 6)) yields

$$\sqrt{n}(\hat{\theta}_2(\hat{\theta}_1) - \theta_0) = \sqrt{n}(\hat{\theta}_2(\theta_{01}) - \theta_0) + \sqrt{n}\nabla \hat{\theta}_2(\theta_{01})(\hat{\theta}_1 - \theta_{01}) + o_p(1).$$

This implies the following i.i.d. decomposition of the two-stage estimator

$$\sqrt{n}(\hat{\theta}_2(\hat{\theta}_1) - \theta_2) = \frac{1}{n} \sum_{i=1}^{n} IF_2(Y_i, X_i, Z_i; \theta_2)$$

$$+ \frac{1}{n} \mathbb{E}[\nabla_\theta U_2(Y, Z, X; \theta_2, \theta_1)]^{-1} \times \mathbb{E}[\nabla_\theta U(Y, Z, X; \theta_2, \theta_1)] \sum_{i=1}^{n} IF_1(X_i, Z_i; \theta_1) + o_p(1)$$

$$= n^{-1/2} \sum_{i=1}^{n} IF_3(Y_i, X_i, Z_i; \theta_2, \theta_1) + o_p(1).$$

By the central limit theorem we obtain that

$$\sqrt{n}(\hat{\theta}_2(\hat{\theta}_1) - \theta_2) \overset{D}{\longrightarrow} N(0, \Sigma),$$

where we can estimate the asymptotic variance by the plug-in estimate

$$\hat{\Sigma} = \frac{1}{n} \sum_{i=1}^{n} IF_3(Y_i, X_i, Z_i; \hat{\theta}_2, \hat{\theta}_1)^{\otimes 2}.$$

As noted in (Parke, 1986), the two influence functions $IF_1$ and $IF_2$ will generally be independent. However, we do not need to exploit this to obtain consistent estimates of the variance.

The case where the stage one model is based on a Gaussian mixture model requires additional considerations. Under the regularity conditions specified in (Redner and Walker, 1984), we obtain the usual rate of convergence such that $\sqrt{n}(\hat{\theta}_1 - \theta_1)$ is asymptotically normal distributed with mean zero. This holds in particular for
the important case, where the conditional distribution in each group is Gaussian and the conditional variance given covariates is fixed across the different groups in the mixture model, i.e., only the intercept of \( \xi_{ki} \), \((\tilde{\alpha}_k)\), varies between groups. It follows that in this case, the necessary regularity conditions for the stage 1 model are full-filled and the derivation of the asymptotic distribution of the proposed two-stage estimator follows along the same lines as in the normal case \( K = 1 \), with the influence function being estimated by the product of the inverse information matrix and score function of the MLE.

5 Simulation study

In this section we explore the finite sample properties of \texttt{2SSEM}. We first considered scenarios where all distributional assumptions of the model were fulfilled. Next, we explored the robustness of the proposed methods in misspecified models and finally we explored \texttt{2SSEM} in a non-parametric setting using a flexible spline model. The Monte Carlo simulations were based on the model illustrated in Figure 1 with the stage 1 model defined as \( \xi_i = \gamma_1 Z_i + \tilde{\zeta}_i \), and \( X_{ij} = \xi_i + \tilde{\epsilon}_{ij} \) and the stage 2 model given by

\[
\eta_i = \beta^T \varphi(\xi_i) + \gamma_2 Z_i + \zeta_i, \quad Y_{ij} = \eta_i + \epsilon_{ij},
\]

with mutually independent residual terms \( \tilde{\zeta}_i, \zeta_i, \tilde{\epsilon}_{ij}, \epsilon_{ij}, j = 1, 2, 3 \). The distribution of these terms was varied throughout the simulations. The parameters of primary interest were the structural parameters, \( \beta \), defining the association between the two latent variables \( \xi_i \) and \( \eta_i \).

5.1 Simulations I: Correctly specified model

Data was generated from a quadratic structural model \( \eta_i = \beta_0 + \beta_1 \xi_i + \beta_2 \xi_i^2 + \gamma_2 Z_i + \zeta_i \), with all residuals \( \tilde{\zeta}_i, \zeta_i, \tilde{\epsilon}_{ij}, \epsilon_{ij}, j = 1, 2, 3 \) being standard normal and \( \beta_0 = 1, \beta_1 = 1, \beta_2 = 0.5 \). The simulation was run with sample sizes of \( n = 1,000 \) and \( n = 500 \) (see Section D), without any covariate in the model \((\gamma_1 = 0, \gamma_2 = 0)\) and with a covariate \((\gamma_1 = 1, \gamma_2 = 1, \) see supplementary material\). The simulation
Table 1: Performance of the estimators: Gaussian 2SSEM, 2SEMM with 2-component mixture (2SSEM mixture), 2SLS, 2SLS with heteroskedasticity standard errors (2SLS robust), methods of moments estimator (2SMM and 2SMM robust, with the former deriving moments from a Gaussian distribution. Standard error are omitted here but are derived in Wall and Amemiya (2000)), and approximate ML (Laplace, AGQ9) in a simulation study from a quadratic model $E(\eta | \xi) = \beta_0 + \beta_1 \xi + \beta_2 \xi^2$ (true parameters $\beta_1 = 1$ and $\beta_2 = 0.5$) where all assumptions hold.

| Method               | Mean     | SD      | SE      | SE SD    | Cov.    | RMSE |
|----------------------|----------|---------|---------|----------|---------|------|
| 2SSEM                | 0.996    | 0.371   | 0.349   | 0.942    | 0.940   | 0.371 |
| 2SSEM mixture        | 1.031    | 0.393   | 0.424   | 1.079    | 0.941   | 0.394 |
| 2SLS                 | 0.975    | 0.647   | 0.606   | 0.938    | 0.938   | 0.647 |
| 2SLS robust          | 0.975    | 0.647   | 0.631   | 0.975    | 0.948   | 0.647 |
| 2SMM                 | 1.031    | 0.431   |         |          |         | 0.432 |
| 2SMM robust          | 1.042    | 0.466   |         |          |         | 0.468 |
| Laplace              | 1.127    | 0.306   | 0.292   | 0.957    | 0.939   | 0.331 |
| AGQ9                 | 1.002    | 0.277   | 0.272   | 0.984    | 0.947   | 0.277 |
| 2SSEM                | 0.499    | 0.072   | 0.068   | 0.944    | 0.933   | 0.072 |
| 2SSEM mixture        | 0.507    | 0.077   | 0.084   | 1.095    | 0.934   | 0.077 |
| 2SLS                 | 0.496    | 0.115   | 0.100   | 0.864    | 0.919   | 0.115 |
| 2SLS robust          | 0.496    | 0.115   | 0.112   | 0.973    | 0.942   | 0.115 |
| 2SMM                 | 0.506    | 0.081   |         |          |         | 0.081 |
| 2SMM robust          | 0.508    | 0.088   |         |          |         | 0.088 |
| Laplace              | 0.526    | 0.060   | 0.057   | 0.958    | 0.939   | 0.065 |
| AGQ9                 | 0.501    | 0.054   | 0.053   | 0.986    | 0.943   | 0.054 |

The study was based on 1,000 replications. The 2SSEM methods were compared to Bollen’s two-stage least squares (2SLS) estimator (Bollen, 1995) (see Section B), 2SMM of Wall and Amemiya (2000), and approximate ML based on a Laplace approximation as well as Adaptive Gaussian Quadrature (AGQ) with 9 quadrature points.

Simulations showed that the 2SSEM estimator had good properties in finite samples (Table 1). The method seemed approximately unbiased and confidence intervals had coverage probabilities close to the nominal level. It is interesting to see that in this case, where residual terms were normal, nothing seemed to have been lost by applying the robust mixture model extension. In addition to providing effectively
unbiased inference this method yielded standard errors that were very close to those obtained assuming normality. As expected, ML analysis was more efficient, but the loss of the \textit{2SSEM} procedure was modest. The Laplace approximation showed some bias compared to the rest of the methods, but preformed well as measured by the RMSE and was almost as efficient as the more sophisticated AGQ-approximation. Bollen’s 2SLS provided unbiased estimation, but it was clearly less efficient than both ML and \textit{2SSEM}. Also, the non-robust standard errors as suggested by Bollen (1995) underestimated the uncertainty in the second order term. The methods of moments estimator 2SMM was less efficient than the \textit{2SSEM} estimator but performed clearly better than 2SLS. The conclusions were consistent across all scenarios we examined (see Section D).

In contrast to 2SLS and 2SMM, our method is not restricted to polynomial structures, and we also examined the performance with an exponential effect, $\eta_i = \beta_1 \xi_i + \beta_2 \exp(\xi_i) + \zeta_i$. The \textit{2SSEM} estimator also performed well in this setting being effectively unbiased with correct coverage of the confidence limits (see Section D for details).

5.2 Simulations II: Robustness

Here we explored the properties of the estimators in misspecified models. First we examined data generating mechanisms identical to the previous model except of the conditional distribution of the latent variable $\xi_i$ which was not Gaussian but followed a mixture distribution, i.e., $\tilde{\zeta}_i \sim 0.25N(0,1) + 0.75N(3,1)$. The results are summarized in Table 2, where we see some bias in the \textit{2SSEM} estimator using a Gaussian distribution for the stage 1 model. The mixture \textit{2SSEM} estimator is unbiased with correct coverage. As an observation, we noted that \textit{2SSEM} was generally much faster, more computational stable and less dependent on starting values than the Laplace and AGQ approximations. This was especially the case in the mixture setting where the ML-methods had convergence problems and need for fine-tuning across different implementations (results not shown).

The above simulation setup corresponds exactly to the assumptions of our mixture model extension, so to test the robustness of the extension we also included a study where $\tilde{\zeta}_i$ followed a uniform distribution with mean zero and variance one, and a
simulation where the residuals of the indicators, \( \tilde{\epsilon}_{ij} \) followed a uniform distribution. In both cases, the 2SSEM mixture estimator was effectively unbiased with coverage close to the nominal level. Interestingly, the Gaussian 2SSEM was robust to the misspecification of the indicator distribution where it performed slightly better than the mixture model. Both 2SLS and 2SMM appeared to be robust to the considered misspecifications. In most cases both estimators were less efficient than 2SSEM (see Section D), however, as the sample size increased we observed that 2SMM seemed to catch up with 2SSEM. We note however, that a severe limitation of the 2SMM approach is the lack of generalizations (and implementations) allowing for example relaxation of conditional independence assumptions, inclusion of covariates, and most importantly specifications of functional forms beyond the polynomial structure.

5.3 Simulations III: Non-parametric estimation

To study 2SSEM in a non-parametric setting, we also simulated data from the measurement models defined in the previous sections but with unknown functional relationship between the latent variables given by \( \varphi(\xi; \beta) = \beta_1 \xi + \beta_2 \xi^2 + \sin(\beta_3 \xi) \). A natural cubic spline with \( k \) knots \( t_1 < t_2 < \ldots < t_k \) is given by \( E(\eta_i \mid \xi_i) = \gamma_0 + \gamma_1 \xi_i + \sum_{j=1}^{k-2} \gamma_{j+1} f_j(\xi_i), \) with \( f_j(\xi_i) = g_j(\xi_i) - \frac{t_k-t_j}{t_k-t_{k-1}} g_{k-1}(\xi_i) + \frac{t_{k-1}-t_j}{t_k-t_{k-1}} g_k(\xi_i), \) \( j = 1, \ldots, k - 2. \) Here \( g_j(\xi_i) = (\xi_i - t_j)^3 1_{\{\xi_i > t_j\}} \) so to apply 2SSEM we calculated \( E[g_j(\xi_i) \mid X_i, Z_i] \) (see Section 3). As a benchmark we compared 2SSEM with the estimator proposed by Kelava et al. (2017) and the corresponding Matlab implementation\(^1\). Here the number of equidistant knots were chosen by dividing the simulated data into a single test and training data of equal size and choosing the spline basis (degrees of freedom varying from 1 to 11) as the one that minimized the RMSE evaluated in the test data. We noted that slightly better results were obtained for 2SSEM when the hyper-parameters (spline knots) were chosen using 5-fold cross validation. To make the results more comparable we, however, adopted the same method for choosing the degrees of freedom for the spline using the exact same split of the testing and training data.

In each simulation, \( r = 1, \ldots, 100 \), we generated \( n = 200 \) observations, and for

\(^1\)https://github.com/tifasch/nonparametric/tree/ead709097d6
each estimator we calculated $\text{RMSE}_r = \left( \sum_{i=1}^{n} [\phi(\xi_i; \beta) - \hat{\phi}(\xi_i; \hat{\gamma}_r)]^2 \right)^{\frac{1}{2}}$, where $\beta$ denotes the true parameter and $\hat{\gamma}_r$ is the estimated parameters of the spline model, i.e., $\hat{\eta} = \check{\phi}(\xi; \check{\gamma}_r) = B(\xi) \check{\gamma}_r$, where $B(\xi)$ is the spline basis design matrix. With $\beta_1 = 1, \beta_2 = 0, \beta_3 = 1$ and with $\check{\zeta}, \zeta \sim \mathcal{N}(0,1)$ the average RMSE over all replications were 0.314 for Kelava’s estimator and 0.112 for 2SSEM, and similarly when $\check{\zeta}, \zeta \sim \mathcal{U}(-6, 6)$ the average RMSE were 0.933 and 0.608 in favour of 2SSEM. Similar conclusions were drawn when using a stronger non-linear functional form given by $\beta_1 = 1, \beta_2 = 0, \beta_3 = 1$. In the Gaussian case the average RMSE was 1.177 and 0.827, and in the uniform case 3.613 and 1.988, all in favour of 2SSEM. In addition, we note that another advantage of the 2SSEM estimator is the immediately available expressions of the asymptotic variance through the estimated influence functions. See Section D.4 for more details.

6 Application: Modelling in vivo brain serotonin measurements

Serotonin (5-HT, 5-hydroxytryptamine) is known to play an important role in the regulation of appetite, sleep, mood, sex, and memory function. Variation in cerebral 5-HT levels is also recognized as being influential on addiction and development of psychiatric disorders such as schizophrenia and depression. With Positron Emission Tomography (PET) techniques it is possible to quantify post and pre-synaptic markers of the serotonergic system in the living human brain, such as the serotonin 2A receptor (5-HT$_{2A}$) and the serotonin transporter (SERT). These markers have been intensively studied and associations to eating, sleeping, and mood disorders (Meyer, 2007; Meyer et al., 1999) have been identified. Animal studies examining the consequence of manipulation of central 5-HT levels indicate an approximate (negative) linear relationship between normal synaptic 5-HT levels and 5-HT$_{2A}$ receptor binding (Licht et al., 2009). It has been suggested that (Meyer, 2007) 5-HT$_{2A}$ receptor binding may act as an indicator of the cerebral 5-HT levels. Similarly, experimental studies have shown that manipulation of synaptic 5-HT levels causes change in the SERT binding (Pineyro et al., 1994) with a suggested non-linear functional form (inverted u-shape where low and high
serotonin levels both are associated with low levels of SERT). This association was studied in (Erritzoe et al., 2010) hypothesizing that underlying low 5-HT levels could lead to a compensatory up-regulation of 5-HT$_{2A}$ receptor binding and down-regulation of SERT.

![Figure 2: Path diagram for a structural equation model describing the relationship between 5-HT$_{2A}$ receptor binding (light grey) and SERT binding (dark grey). Each of the two types of markers are described by a single latent variable. For the 5-HT$_{2A}$ receptor the following regions (light grey regions in the glass brain of the right figure) was chosen as measurements: Parietal cortex (pac), Superior frontal cortex (sfc), Posterior cingulate gyrus (pci), and Anterior cingulate gyrus (aci). For the serotonin transporter we chose the regions: Putamen (put), Insula (ins), Midbrain (mid), Thalamus (th).](image)

We will here present an analysis of the same sample as in the original paper, while taking into account the measurement error in both the 5-HT$_{2A}$ and SERT measurements by using a non-linear SEM. The 5-HT$_{2A}$ receptor binding potential (BP$_p$) and the SERT binding potential (BP$_{ND}$) was measured in 56 normal subjects. For each subject, the measurements were summarized in a number of regions of interest. We refer to the original paper for details on the method used in acquiring the data.

For the serotonergic markers the concept of a measurement model seems to be ideal in capturing the idea of an underlying common regulator of the two types of
measurements. For the 5-HT\textsubscript{2A} receptor outcome in a given region, we will assume a model

\[ \text{BP}_{p,\text{ROI}} = \mu_{\text{ROI}} + \lambda_{\text{ROI}} \cdot \xi + \epsilon_{\text{ROI}}, \]

(26)

with a single latent variable \( \xi \). The flexibility in letting each region have its own intercept, \( \mu_{\text{ROI}} \), loading parameter, \( \lambda_{\text{ROI}} \), and residual term \( \epsilon_{\text{ROI}} \sim \mathcal{N}(0, \sigma^2_{\text{ROI}}) \) allows us to model data, where different regions have different degrees of binding potential, variation and correlation with other regions. We will assume independence between residuals though this is not a necessary assumption. We propose a similar model for SERT binding with a measurement model described by a latent variable \( \eta \). For both markers we chose 4 high binding regions of interest which previously have been demonstrated to be reliable measurements of 5-HT\textsubscript{2A} and SERT binding, respectively (see Figure 2). To describe the association between 5-HT\textsubscript{2A} receptor binding and SERT binding we added a simple structural model \( \eta = \mu_{\text{sex}} + \beta \xi + \zeta \), to see how well a linear approximation would describe the relationship. In this simple model, \( \xi \) takes the role of the common regulator, i.e. the central 5-HT level, as measured directly by the 5-HT\textsubscript{2A} receptor binding, and the common regulator predicts the levels of the global SERT variable \( \eta \).

We estimated the parameters of the model using ML. The estimate of the primary parameter of interest, \( \beta \), was 0.046 BP\textsubscript{ND}/BP\textsubscript{p} (with parietal cortex and thalamus as reference regions, allowing us to interpret the effect as change in SERT BP\textsubscript{p} in thalamus per unit change in parietal cortical BP\textsubscript{ND}) and 95% CI [−0.057; 0.149]. The lack of statistical significance may be explained by the lack of non-linear effects in our model specification. A \( \chi^2 \) omnibus-test of goodness-of-fit (a likelihood ratio test against an unstructured 8-dimensional normal distribution) yielded a \( p \)-value of 0.23. Thus, based solely on this test there was no evidence against the model. Clearly, this goodness-of-fit test is, however, not adequate for detecting non-linearities (Mooijaart and Satorra, 2009).

Next, we applied the 2SSEM procedure to the structural equation model of Figure 2 with the association between \( \xi \) and \( \eta \) described by a second order polynomial: \( \eta = \mu_{\text{sex}} + \beta_1 \xi + \beta_2 \xi^2 + \zeta \). The estimates were \( \hat{\beta}_1 = 0.676 \) (95% CI [0.321; 1.030], \( p = 0.00018 \)) and \( \hat{\beta}_2 = -0.153 \) (95% CI [−0.233; −0.074], \( p = 0.0002 \)), thus
confirming our hypothesis of a non-linear association between 5-HT$_{2A}$ receptor and SERT binding potential (Wald test for the hypothesis of no association: $p = 0.0008, df = 2$).

A more flexible natural cubic spline model was next applied. The predicted latent variable of the measurement error model for 5-HT$_{2A}$ receptor binding potential was in the range 0.5-3.5 BP$_p$, and we choose 4 knot points equidistantly in the interval 1 to 3. The association between the two markers (and comparison with the linear and quadratic model) is shown in Figure 3. The natural cubic spline suggests a more flat association between 5-HT$_{2A}$ BP$_p$ and SERT BP$_{ND}$ for high 5-HT$_{2A}$ binding potential values, but otherwise there was a close agreement with the quadratic model. We conducted a more formal comparison of the two models using 5-fold cross validation with all indicator variables normalized. The RMSE
was in slight favour of the quadratic model (0.94 vs 1.03). We also examined natural cubic splines with increased number of knots, but they all exhibited overfitting with higher RMSE. Finally, we used a two-component mixture in the stage one model and got results that were almost identical to those of the Gaussian model. Also, as in the original paper we observed that the estimated non-linear association was not sensitive to removing the observations with the highest values of 5-HT$_{2A}$ binding potential from the data (results not shown). Thus, in agreement with animal and experimental studies, we were able to show a non-linear association between these two serotonergic markers. Our refined analysis also confirmed the findings of the original paper (Erritzoe et al., 2010), where the same data was analysed using standard regression techniques and hence results are likely to be susceptible to bias due to measurement error in both variables.

7 Discussion

ML-inference in non-linear SEMs is complex. Computational intensive methods based on numerical integration are needed and results are sensitive to distributional assumptions. This paper presented the two-stage estimator 2SSEM as a computationally simple alternative to ML. Here both steps are based on linear models: first we predict the non-linear terms and then these are related to latent outcomes in the second step. We identified the asymptotic distribution of 2SSEM, developed a robust extension based on mixture models and implemented the methods in a user-friendly R-package (see Appendix C). Simulations indicated a modest loss of efficiency compared to ML-estimation and our method was shown to be more powerful than two computationally simple and robust alternatives, i.e., 2SLS and 2SMM. In addition, 2SSEM can be applied to a larger class of non-linear functions than 2SLS and 2SMM. In particular the class of restricted cubic splines is an important example which have shown to be very useful in applications of regression models. The introduction of stable and fast estimation algorithms for spline functions in the structural equation framework is likely to lead to important improvements in applications which for too long have been restricted to linear relationships.

In linear models, 2SSEM is equivalent to regression calibration (Carroll et al., 2006).
This method has been investigated in linear SEMs e.g. by Skrondal and Laake (2001) and Sánchez et al. (2009a). In non-linear SEMs, the idea of using mixture modelling to achieve more robust estimation has been exploited for ML-estimators e.g. by Kelava et al. (2014). The handling of splines in 2SSEM is related to the non-parametric estimators suggested by Carroll et al. (1999) for linear regression models with measurement error in covariates. Bayesian methods have been developed for semi-parametric estimation in SEMs (Song et al. (2013), Guo et al. (2012), Kelava and Brandt (2014)), but frequentist methods are rare. Bauer (2005) and Kelava et al. (2017) presented interesting methods but did not provide results on asymptotic standard errors. The latter procedure was included in our simulation study where it yielded larger prediction errors than 2SSEM.

The two-stage approach may be especially useful in data bases with many different research projects. Here the SEM for the exposure may be fitted only once and the predicted non-linear terms can be stored along with the influence function. Then the predictions of exposure terms can be related to different outcomes by different research groups using linear structural models with corrected standard errors. Even in situations where ML-inference is the goal, 2SSEM will likely be very useful in providing good starting values.

When using 2SSEM for assessing associations between latent variables an obvious strategy would be to start the analysis with a rich parametric model (e.g., spline model) which may then be reduced by backward selection using Wald tests. An obvious extension would be to develop lasso-type regularization for the 2SSEM estimator. Similarly, different parametric forms may be compared using Wald tests in a nested model. An alternative is to base the model selection on the estimated out-of-sample predictive performance through cross-validation as demonstrated in the application. It may also be possible to develop fit criteria to detect general non-linear misfit. Recent theory in non-linear SEMs have focused on the development of such criteria and it may be possible to extend these so that they can be used together with 2SSEM. For example, Schermelleh-Engel et al. (2014) developed a $\chi^2$-test comparing the observed and expected covariance matrix of the observed variables appended with selected products of indicators. Another interesting possibility would be to consider cumulative residuals as described by Sánchez et al. (2009b) for linear SEMs.
We applied non-linear models to PET measurements of the serotonergic system. Based on biological evidence we proposed a statistical model describing the underlying cerebral 5-HT level by inclusion of latent components in a SEM. The underlying 5-HT level were here assumed to be measured indirectly by PET measurements of 5-HT$_{2A}$ receptor binding and serotonin transporter binding. In agreement with animal and experimental studies, we were able to show a non-linear association between these two serotonergic markers. Our model represents a first step towards linking several measurements of the serotonergic system into a simultaneous description of central 5-HT levels. An interesting longer-term perspective of this model is the possibility to explore the association between latent 5-HT levels and the development of neuropsychiatric diseases such as major depressive episodes. The extension of 2SSEM to allow for binary and time-to-event endpoints will be a topic for future research.

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|                | Mean  | SD    | SE    | SD/SE | Cov.   | RMSE |
|----------------|-------|-------|-------|-------|--------|------|
|                | 2SSEM | 2SSEM mixture | 2SLS robust | 2SMM | 2SMM robust |
| **$\tilde{\zeta} \sim GMM$** |       |       |       |       |        |      |
| $\beta_1 = 1$ | 1.349 | 0.088 | 0.086 | 0.976 | 0.021 | 0.360 |
|                | 1.000 | 0.104 | 0.103 | 0.988 | 0.948 | 0.104 |
|                | 1.012 | 0.169 | 0.162 | 0.956 | 0.936 | 0.170 |
|                | 1.000 | 0.112 |       |       | 0.112  |      |
|                | 0.999 | 0.114 |       |       | 0.114  |      |
| $\beta_2 = 0.5$ |       |       |       |       |        |      |
|                | 0.380 | 0.030 | 0.029 | 0.976 | 0.025 | 0.123 |
|                | 0.499 | 0.038 | 0.038 | 0.990 | 0.947 | 0.083 |
|                | 0.496 | 0.056 | 0.055 | 0.976 | 0.929 | 0.056 |
|                | 0.500 | 0.040 |       |       | 0.040  |      |
|                | 0.500 | 0.041 |       |       | 0.041  |      |
| **$\tilde{\zeta} \sim Unif$** |       |       |       |       |        |      |
| $\beta_1 = 1$ | 0.998 | 0.069 | 0.069 | 0.998 | 0.948 | 0.069 |
|                | 0.998 | 0.075 | 0.075 | 1.007 | 0.957 | 0.075 |
|                | 1.003 | 0.085 | 0.087 | 1.015 | 0.959 | 0.086 |
|                | 1.001 | 0.078 |       |       | 0.078  |      |
|                | 1.001 | 0.077 |       |       | 0.077  |      |
| $\beta_1 = 0.5$ |       |       |       |       |        |      |
|                | 0.310 | 0.054 | 0.056 | 1.030 | 0.102 | 0.198 |
|                | 0.485 | 0.101 | 0.104 | 1.027 | 0.944 | 0.102 |
|                | 0.489 | 0.160 | 0.159 | 0.994 | 0.934 | 0.161 |
|                | 0.544 | 0.124 |       |       | 0.131  |      |
|                | 0.520 | 0.126 |       |       | 0.128  |      |
| **$\tilde{\epsilon}_j \sim Unif$** |       |       |       |       |        |      |
| $\beta_1 = 1$ | 0.997 | 0.075 | 0.075 | 1.002 | 0.945 | 0.075 |
|                | 0.998 | 0.082 | 0.082 | 1.000 | 0.935 | 0.082 |
|                | 0.997 | 0.090 | 0.091 | 1.014 | 0.951 | 0.090 |
|                | 1.000 | 0.079 |       |       | 0.079  |      |
|                | 1.000 | 0.079 |       |       | 0.079  |      |
| $\beta_1 = 0.5$ |       |       |       |       |        |      |
|                | 0.506 | 0.063 | 0.063 | 0.996 | 0.951 | 0.063 |
|                | 0.521 | 0.072 | 0.076 | 1.055 | 0.956 | 0.075 |
|                | 0.499 | 0.088 | 0.088 | 0.996 | 0.937 | 0.088 |
|                | 0.521 | 0.070 |       |       | 0.073  |      |
|                | 0.512 | 0.074 |       |       | 0.074  |      |

Table 2: Performance of the two-stage estimator assuming a Gaussian distribution (2SSEM) and with 2-component mixture (2SSEM mixture) in a simulation study from a quadratic model in three scenarios, where modelling assumptions were not all satisfied. First the latent predictor followed a two-component mixture distribution, then the latent predictor followed a uniform distribution and finally the residuals in the measurement model of stage one followed a uniform distribution.
A General proof of consistency and robustness to direct associations between stage one and stage two model

In this section, we prove that two-stage estimation is consistent also in the situation where some covariates may have direct effects on the outcomes of the stage 2 model \((K \neq 0)\). We also show that the two-stage estimator can be modified to yield consistent estimation in situations where there are direct effects of outcomes in the stage 1 model on outcomes in the stage 2 model.

**Theorem 2.** Under the assumptions of the non-linear structural equation model with \(K \neq 0\), the two-stage estimator will yield consistent estimation of all parameters \((\theta)\) except for the residual covariance, \(\Psi\), of the latent variables in step 2.

**Proof.** Since the exposure part of the model is correctly specified \(\theta_1\) is estimated using ML-estimation in the marginal distribution of \(X\) given \(Z\) and therefore \(\hat{\theta}_1\) is consistent under mild regularity conditions (Anderson and Amemiya, 1988).

In step 2, the model is misspecified as we fit a linear model to a non-linear association. In a linear SEM, the estimator will converge to the parameter value inducing the modelled mean and covariance which is closest to the true mean and covariance White (1982). We prove the theorem by showing that even though the model is misspecified it includes the true mean and covariance of the data. Therefore, \(\hat{\theta}_2\) will converge to the parameter value which induces the true mean and variance. Finally, this value is characterized and it is seen to be identical to the truth \((\theta_2)\) except for elements describing the residual covariance of the latent variables in step 2 \((\Psi)\).

In step 2, we fit a linear model to the data \(V_i = (Z_i^t, \varphi^*(\xi_i)^t, Y_i^t)^t\). It is assumed that this model has the correct measurement part \((Y_i = \nu_2 + \Lambda_2\eta_i + K_2Z_i + \epsilon_i)\). Here the subscript 2 is used to distinguish the parameters of model 2 from the true parameter value (no subscript). The structural model is: \(\eta_i = \alpha_2 + B_2\varphi^*(\xi_i) + \alpha_2\).
\[ \Gamma_2 Z_i + \zeta_i. \] Using standard results from linear models Bollen (1989), we now derive expressions for the modelled mean and variance

\[
\mu_{V_i} = [\mu_Z, \mu_\varphi, \nu_2 + \Lambda_2 \alpha_2 + \Lambda_2 B_2 \mu_\varphi + (\Lambda_2 B_2 + K_2) \mu_Z]
\]  (27)

\[
\Sigma_{V_i} = \begin{pmatrix}
\Sigma_Z & \Sigma_{Z,\varphi} & [\Sigma_{\varphi,Z}\Gamma_2^t] \Lambda_2^t + \Sigma_2 K_2^t \\
. & \Sigma_\varphi & [\Sigma_{\varphi}\Gamma_2^t] \Lambda_2^t + \Sigma_{\varphi,Z} K_2^t \\
. & . & \Lambda_2 \Sigma_\eta \Lambda_2^t + \Lambda_2 \Gamma_2 \Sigma_2 K_2^t + K_2 \Sigma_2 \Gamma_2^t \Lambda_2^t + \Lambda_2 B_2 \Sigma_{\varphi,Z} K_2^t + K_2 \Sigma_2 \varphi, \varphi \Lambda_2^t + K_2 \Sigma_2 \varphi, Z \Lambda_2^t + \Omega_2
\end{pmatrix}
\]  (28)

where \( \Sigma_\eta = B_2 \Sigma_{\varphi} \Gamma_2^t + B_2 \Sigma_{\varphi,Z} \Gamma_2^t + \Sigma_2 \varphi, \varphi \Gamma_2^t + \Sigma_2 \varphi, Z \Gamma_2^t + \Psi_2 \) is the modelled variance of \( \eta \) and \( \mu_\varphi, \mu_Z, \Sigma_\varphi, \Sigma_{\varphi,Z}, \Sigma_Z \) are completely unstructured parameters modelling the mean and variance of the step-two covariates \( (\varphi^*(\xi_i), Z) \).

To calculate the true mean and variance of \( V_i \) we re-write the structural model as

\[
\eta_i = \alpha + B \varphi(\xi_i) + \Gamma Z_i + \zeta_i \]
\[
= \alpha + B \varphi^*(\xi_i) + B [\varphi(\xi_i) - \varphi^*(\xi_i)] + \Gamma Z_i + \zeta_i,
\]  (29)

From the law of iterated expectations it follows that \( \mathbb{E} [\varphi(\xi_i) - \varphi^*(\xi_i)] = 0 \) and therefore the marginal mean of the data is

\[
\mathbb{E}\{V_i\} = [\mathbb{E}(Z_i), \mathbb{E}\{\varphi(\xi_i)\}, \nu + \Lambda \alpha + \Lambda B \mathbb{E}\{\varphi(\xi_i)\} + (\Lambda \Gamma + K) \mathbb{E}(Z_i)]
\]  (30)

For calculation of the variance, we first derive variance of the latent variable \( \eta_i \) again using equation (29)

\[
\text{Var}(\eta_i) = B \text{Var}[\varphi^*(\xi_i)] B^t + B \text{Cov}[\varphi^*(\xi_i), Z_i] \Gamma^t + \Gamma \text{Cov}[Z_i, \varphi^*(\xi_i)] B^t
\]
\[
+ B \text{Var}[\varphi(\xi_i) - \varphi^*(\xi_i)] B^t + \Gamma \text{Var}(Z_i) \Gamma^t + \Psi.
\]  (31)

because \( \text{Cov}[\varphi^*(\xi_i), \varphi(\xi_i) - \varphi^*(\xi_i)] = 0 \) and \( \text{Cov}[Z_i, \varphi(\xi_i) - \varphi^*(\xi_i)] = 0 \), which again follows from the law of iterated expectations.
Now the variance of the step-two data is

\[
\Var[V_i] = \\
\begin{pmatrix}
\Var(Z_i) & \Cov(Z_i, \varphi^*(\xi_i)) & [\Cov(\varphi^*(\xi_i), Z_i)B^t + \Var(Z_i)\Gamma^t]\Lambda^t + \Var(Z_i)K^t \\
. & \Var[\varphi^*(\xi_i)] & [\Var(\varphi^*(\xi_i))B^t + \Cov(\varphi^*(\xi_i), Z_i)\Gamma^t]\Lambda^t + \Cov(\varphi^*(\xi_i), Z_i)K^t \\
. & . & \Var(Y_i)
\end{pmatrix}
\]

(32)

where \(\Var(Y_i) = \Lambda \Var(\eta_i)\Lambda^t + \Lambda \Gamma \Var(Z_i)K^t + K \Var(Z_i)\Gamma^t\Lambda^t + \Lambda B \Cov[\varphi^*(\xi_i), Z_i]K^t + K \Cov[Z_i, \varphi^*(\xi_i)]B^t\Lambda^t + K \Var(Z_i)K^t + \Omega\). Here we used \(\Cov[\varphi^*(\xi_i), Y_i] = \Cov[\varphi^*(\xi_i), \Lambda \eta_i] = \Cov[\varphi^*(\xi_i), B \varphi^*(\xi_i) + \Gamma Z_i]\Lambda^t\) as \(\Cov[\varphi^*(\xi_i), \varphi(\xi_i) - \varphi^*(\xi_i)] = 0\) and \(\Cov(Z_i, Y_i) = \Cov(Z_i, \Lambda \eta_i) = \Cov(Z_i, B \varphi^*(\xi_i) + \Gamma Z_i)\Lambda^t\) as \(\Cov(Z_i, \varphi(\xi_i) - \varphi^*(\xi_i)] = 0\).

Now it is straightforward to see that the modelled mean and covariance is equal to the corresponding true values \([(27) = (30)\) and \((28) = (32)\)] if \(B_2 = B, \Lambda_2 = \Lambda, \Gamma_2 = \Gamma, \Omega_2 = \Omega, \alpha_2 = \alpha, \nu_2 = \nu, \mu_\varphi = \mathbb{E}[\varphi(\xi_i)], \mu_Z = \mathbb{E}(Z_i), \Sigma_{Z, \varphi} = \Cov(Z_i, \varphi^*(\xi_i)], \Sigma_{\varphi} = \Var[\varphi^*(\xi_i)], \Sigma_Z = \Var(Z_i)\) and \(\Psi_2 = \Psi + B \Var[\varphi(\xi_i) - \varphi^*(\xi_i)]B^t\). Note that, although the expression for the modelled variance of the latent variable \((\Sigma_{\varphi})\) is missing the term \(B \Var[\varphi(\xi_i) - \varphi^*(\xi_i)]B^t\), the model can achieve the correct variance of \(Y_i\) by adding the missing term to the residual variance \(\Psi_2\). Since the model includes the true mean and variance, \(\hat{\theta}_2\) will converge to the specific parameter value inducing the true mean and variance. This means that all parameters are consistently estimated except for the variance of the latent variable, which will be overestimated.

The above arguments were made for predicted values \(\varphi^*\). The results now follow from the Continuous Mapping Theorem and by noting that \(\varphi^*_n \to \varphi^*\) a.s. as \(n \to \infty\).

\[\square\]

**Corollary 1.** Consider a model where there may be direct effects of response variables in the stage 1 model on response variables in the stage 2 model (see Figure 4), i.e., the measurement model of stage-two data is \(Y_i = \nu + \Lambda \eta_i + KZ_i + LX_i + \epsilon_i\). Consistent estimation can be obtained with the two-stage estimator if the measurement model for \(Y_i\) is correctly specified, i.e., \(X_i\) is included in the stage 2 analysis.
as additional covariates.

Proof. The stage-one model is correctly specified so this stage remains consistent. According to Theorem 2, the second stage analysis is also consistent when some covariates have direct effects on the response variables. The only requirement is that these covariates are also included in the first stage analysis, so that \( \text{Cov}[\varphi(\xi_i) - \varphi^*(\xi_i), Z_i] = 0 \). Response variables in stage one are of course a part of the stage one analysis. A consequence of this is that \( \text{Cov}[\varphi(\xi_i) - \varphi^*(\xi_i), X_i] = 0 \) and therefore the stage two analysis is consistent.

\[ \]

Figure 4: Path diagram showing an example of the non-linear structural equation model with a direct effect of an indicator variable of the stage one model onto a variable in the stage two model.

\[ \]

Bollen’s IV method

The idea is to replace latent variables with observed reference variables and then estimate parameters using regression techniques. For illustration, we use our simulation model with a linear structural equation \( \eta = \alpha + \beta \xi + \zeta \). If we use \( Y_1 \) and \( X_1 \) as reference indicators, we can replace the latent variables with observed reference
indicators yielding $Y_1 = \alpha + \beta X_1 - \beta \tilde{\epsilon}_1 + \epsilon_1 + \zeta$. This creates an observed-variable-equation, where predictors are correlated with error terms and therefore least squares estimation would be biased, but a consistent analysis can be performed by using non-reference indicators as instrumental variables. In our example the indicators $X_2$ and $X_3$ could be used as instruments for $X_1$. In linear models, Bollen have shown that this IV-estimator is more robust to model misspecification than ML-analysis (Bollen et al., 2007). He has also extended the method to non-linear models (Bollen (1995); Bollen and Paxton (1998)). Here instrumental variables must be identified for the non-linear terms and this may be challenging. For a quadratic model ($\eta = \alpha + \beta \varphi(\xi) + \zeta$ with $\varphi(\xi) = \xi^2$), Bollen showed that consistent estimation can be achieved by replacing $\xi$ by $X_1$ and by using transformed variables $X_2^2$ and $X_3^2$ as instruments for the non-linear effect term. It is not clear that this procedure would generally yield consistent estimation, but for product and quadratic terms, where $\varphi(X_1 - \hat{\epsilon}_1) = \varphi(X_1) + \varphi_1(X_1, \hat{\epsilon}_1)$, the observed-variable-equation takes the form $Y_1 = \alpha + \beta \varphi(X_1) + \text{error}$, and IV estimation will be consistent as long as it is possible to find instrumental variables that are uncorrelated with the error term. For standard errors, Bollen proposed the usual IV-solution, which in our example takes the form $\hat{\sigma}_e^2(\hat{X}^t\hat{X})^{-1}$, where $\hat{X}$ is $n \times 2$-matrix with an intercept column of ones and a column of predicted values of $X_1$ obtained from a regression on $X_2, X_3$, while $\hat{\sigma}_e^2 = \sum_{i=1}^n u_i^2/n$ with residuals $u_i = Y_{i1} - \hat{\alpha} - \hat{\beta} X_{i1}$. However, this expression assumes homoskedastic errors, which is generally not satisfied in non-linear SEMs. For example in the quadratic model, the observed-variable-equation becomes $Y_1 = \alpha + \beta X_1^2 - \beta \tilde{\epsilon}_1 X_1 + \beta \tilde{\epsilon}_1^2 + \epsilon_1 + \zeta$ and the error term ($\beta \tilde{\epsilon}_1 X_1 + \beta \tilde{\epsilon}_1^2 + \epsilon_1 + \zeta$) will have a variance that depends on $X_1$. Instead, we suggest using the heteroskedasticity robust standard errors for the IV (Wooldridge, 2010), i.e. $(\hat{X}^t\hat{X})^{-1}\hat{X}^tS\hat{X}(\hat{X}^t\hat{X})^{-1}$, where $S$ is a diagonal matrix of squared residuals ($u_i^2$).
C Software implementation

The two-stage estimator is implemented in the lava package in the statistical software R citep:Rlang. The source code is hosted at GitHub and can be downloaded freely from https://github.com/kkholst/lava. The version on which this paper is based on (doi: 10.5281/zenodo.1411865) can be installed with the following command (depending on the devtools package available from CRAN):

\begin{verbatim}
devtools::install_github("kkholst/lava", ref="twostage")
\end{verbatim}

To demonstrate the syntax we simulate from the following measurement models (see Figure ref:fig:lvm1)

\begin{align*}
X_j &= \eta_1 + \epsilon_j, \quad j = 1, 2, 3 \\
Y_j &= \eta_2 + \epsilon_j', \quad j = 1, 2, 3
\end{align*}

(33)

and with a structural model given by

\begin{align*}
\eta_2 &= f(\eta_1) + Z + \zeta_2 \\
\eta_1 &= Z + \zeta_1
\end{align*}

(34) (35)

Figure 5: Path diagram of the simulation model specified by (33)-(35). label:fig:lvm1
with iid measurement errors $\epsilon_{x,j}, \epsilon_{y,j}, \zeta_1, \zeta_2 \sim \mathcal{N}(0,1), j = 1, 2, 3$. and standard normal distributed covariate $Z$. To simulate from this model we use the following syntax:

```
library("lava")
```

```
lava version 1.6.3
```

```
f <- function(x) cos(1.25*x) + x - 0.25*x^2
m <- lvm(x1+x2+x3 ~ eta1, y1+y2+y3 ~ eta2, latent=~eta1+eta2)
regression(m) <- eta1+eta2 ~ z
functional(m, eta2~eta1) <- f
d <- sim(m, n=200, seed=42)  # Default is all parameters are 1
```

We refer to cite:holstjoergensenlava for details on the syntax for model specification. Given the data the first step is now to specify the measurement models in (ref:ex:measurements):

```
m1 <- lvm(x1+x2+x3 ~ eta1, eta1 ~ z, latent=~eta1)
m2 <- lvm(y1+y2+y3 ~ eta2, eta2 ~ z, latent=~eta2)
```

Next, we specify a quadratic relationship between the two latent variables

```
nonlinear(m2, type="quadratic") <- eta2 ~ eta1
```

and the model can then be estimated using the two-stage estimator

```
e1 <- twostage(m1, m2, data=d)
e1
```

|                | Estimate | Std. Error | Z-value | P-value |
|----------------|----------|------------|---------|---------|
| Measurements:  |          |            |         |---------|
| y2-eta2        | 0.97686  | 0.03451    | 28.30865| <1e-12  |
| y3-eta2        | 1.04485  | 0.03485    | 29.98153| <1e-12  |
| Regressions:    |          |            |         |---------|

```
eta2-z  0.88513  0.20778  4.25997  2.045e-05
eta2-eta1_1  1.14072  0.17410  6.55194  5.679e-11
eta2-eta1_2 -0.45055  0.07161 -6.29199  3.134e-10

Intercepts:
y2     -0.12198  0.10915 -1.11749  0.2638
y3     -0.09879  0.10545 -0.93680  0.3489
eta2   0.67814  0.17363  3.90567  9.397e-05

Residual Variances:
y1     1.30730  0.17743  7.36790
y2     1.11056  0.14478  7.67064
y3     0.80961  0.13203  6.13219
eta2   2.08483  0.28985  7.19274

We see a clear statistically significant effect of the second order term (eta2-eta1_2).
For comparison, we can also estimate the full MLE of the linear model:

```r
# Estimate linear model
e0 <- estimate(regression(m1%++%m2, eta2-eta1), d)
result <- estimate(e0, keep="^eta2-[^a-z]", regex=TRUE) # Extract coef. matching reg.ex.
```

| Estimate  | Std.Err | 2.5% | 97.5% | P-value |
|-----------|---------|------|-------|---------|
| eta2-eta1 | 1.4140  | 0.2261 | 0.97083 | 1.857 | 4.014e-10 |
| eta2-z    | 0.6374  | 0.2778 | 0.09291 | 1.182 | 2.177e-02 |

Next, we calculate predictions from the quadratic model using the estimated parameter coefficients

\[ \mathbb{E}_{\eta_2} (\eta_2 | \eta_1, Z = 0), \]

```r
# Predictions
newd <- expand.grid(eta1=seq(-4, 4, by=0.1), z=0)
pred1 <- predict(e1, newdata=newd, x=TRUE)
head(pred1)
```

| y1        | y2        | y3        | eta2 |
|-----------|-----------|-----------|------|
| [1,]      | -11.093569| -10.958869| -11.689950| -11.093569 |
| [2,]      | -10.623561| -10.499736| -11.198861| -10.623561 |
| [3,]      | -10.162565| -10.049406| -10.71787 | -10.162565 |
To obtain a potential better fit we next proceed with a natural cubic spline

```
kn <- seq(-3,3,length.out=5)
nonlinear(m2, type="spline", knots=kn) <- eta2 - eta1
e2 <- twostage(m1, m2, data=d)
```

| Measurements: | Estimate | Std. Error | Z-value | P-value |
|---------------|----------|------------|---------|---------|
| y2-eta2       | 0.97752  | 0.03455    | 28.29248| <1e-12  |
| y3-eta2       | 1.04508  | 0.03488    | 29.96248| <1e-12  |

| Regressions:  | Estimate | Std. Error | Z-value | P-value |
|---------------|----------|------------|---------|---------|
| eta2-z        | 0.86729  | 0.20273    | 4.27795 | 1.886e-05|
| eta2-eta1_1   | 2.86231  | 0.67270    | 4.25495 | 2.091e-05|
| eta2-eta1_2   | 0.00344  | 0.10097    | 0.03409 | 0.9728   |
| eta2-eta1_3   | -0.26270 | 0.29398    | -0.89360| 0.3715   |
| eta2-eta1_4   | 0.50778  | 0.35191    | 1.44293 | 0.149    |

| Intercepts:   | Estimate | Std. Error | Z-value | P-value |
|---------------|----------|------------|---------|---------|
| y2            | -0.12185 | 0.10922    | -1.11563| 0.2646   |
| y3            | -0.09874 | 0.10545    | -0.93638| 0.3491   |
| eta2          | 1.83814  | 1.66416    | 1.10454 | 0.2694   |

| Residual Variances: | Estimate | Std. Error | Z-value | P-value |
|---------------------|----------|------------|---------|---------|
| y1                  | 1.31286  | 0.17750    | 7.39647 |         |
| y2                  | 1.10412  | 0.14465    | 7.63850 |         |
| y3                  | 0.81124  | 0.13185    | 6.15286 |         |
| eta2                | 1.99404  | 0.27004    | 7.38416 |         |

Confidence limits can be obtained via the Delta method using the `estimate` method:

```
p <- cbind(eta1=newd$eta1,
            estimate(e2,f=function(p) predict(e2,p=p,newdata=newd))$coefmat)
head(p)
```
| eta1 | Estimate | Std.Err | 2.5%  | 97.5%   | P-value     |
|------|----------|---------|-------|---------|-------------|
| p1   | -4.0     | -9.611119 | 1.2650975 | -12.09066 | -7.131573   | 3.027543e-14 |
| p2   | -3.9     | -9.324887 | 1.2054915 | -11.68761 | -6.962167   | 1.031268e-14 |
| p3   | -3.8     | -9.038656 | 1.1467339 | -11.28621 | -6.791099   | 3.219580e-15 |
| p4   | -3.7     | -8.752425 | 1.0889618 | -10.88675 | -6.618099   | 9.176275e-16 |
| p5   | -3.6     | -8.466193 | 1.0323409 | -10.48954 | -6.442842   | 2.384613e-16 |
| p6   | -3.5     | -8.179962 | 0.9770711 | -10.09499 | -6.264938   | 5.668675e-17 |

The fitted function can be obtained with the following code (see Figure ref:fig:pred2b):

```r
plot(I(eta2-z) ~ eta1, data=d, col=Col("black",0.5), pch=16,
     xlab=expression(eta[1]), ylab=expression(eta[2]), xlim=c(-4,4))
lines(Estimate ~ eta1, data=as.data.frame(p), col="darkblue", lwd=5)
confband(p[,1], lower=p[,4], upper=p[,5], polygon=TRUE,
        border=NA, col=Col("darkblue",0.2))
```

Figure 6: Estimated association between $\eta_1$ and $\eta_2$ using natural cubic spline (4 knot points) with point-wise 95% confidence limits. label:fig:pred2b
C.1 Cross-validation

A more formal comparison of the different models can be obtained by cross-validation. Here we specify linear, quadratic and cubic spline models with 4 and 9 degrees of freedom.

```r
m2a <- nonlinear(m2, type="linear", eta2~eta1)
m2b <- nonlinear(m2, type="quadratic", eta2~eta1)
kn1 <- seq(-3,3,length.out=5)
kn2 <- seq(-3,3,length.out=8)
m2c <- nonlinear(m2, type="spline", knots=kn1, eta2~eta1)
m2d <- nonlinear(m2, type="spline", knots=kn2, eta2~eta1)
```

To assess the model fit average RMSE is estimated with 5-fold cross-validation repeated two times

```r
## Scale models in stage 2 to allow for a fair RMSE comparison
d0 <- d
for (i in endogenous(m2))
d0[,i] <- scale(d0[,i],center=TRUE,scale=TRUE)
## Repeated 5-fold cross-validation:
ff <- lapply(list(linear=m2a,quadratic=m2b,spline4=m2c,spline6=m2d),
  function(m) function(data,...) twostage(m1,m,data=data,stderr=False,control=list(start=coef(e0),constrain=TRUE)))
fit.cv <- cv(ff,data=d,K=5,rep=2,mc.cores=4,seed=1)
fit.cv
```

| RMSE       |
|------------|
| linear     | 4.508896 |
| quadratic  | 3.270908 |
| spline4    | 3.105159 |
| spline6    | 3.376329 |

Here the RMSE is in favour of the splines model with 4 degrees of freedom (see Figure ref:fig:multifit).

```r
fit <- lapply(list(m2a,m2b,m2c,m2d),
  function(x) {
    e <- twostage(m1,x,data=d)
    pr <- cbind(eta1=newd$eta1,predict(e,newdata=newd$eta1,x=TRUE))
  })
```
```r
return(list(estimate=e, predict=as.data.frame(pr)))
```

```r
plot(I(eta2-z) ~ eta1, data=d, col=Col("black",0.5), pch=16,
    xlab=expression(eta[1]), ylab=expression(eta[2]), xlim=c(-4,4))
col <- c("orange","darkred","darkgreen","darkblue")
lty <- c(3,4,1,5)
for (i in seq_along(fit)) {
  with(fit[[i]]$pr, lines(eta2 ~ eta1, col=col[i], lwd=4, lty=lty[i ]))
}
legend("bottomright",
  c("linear","quadratic","spline(df=4)","spline(df=6)"),
  col=col, lty=lty, lwd=3)
```

Figure 7: Comparison of model fit using linear, quadratic and natural splines models with 4 and 6 degrees of freedom. The points show the actual latent variables. label:fig:multifit

For convenience, the function `twostageCV` can be used to do the cross-validation. For example,
```
setmod <- twostageCV(m1, m2, data=d, df=2:6, nmix=1:3,
                   nfolds=5, rep=1, mc.cores=parallel::detectCores())
```

applies 5-fold cross-validation to select the best splines with degrees of freedom varying from 1-6 (the linear model is automatically included)

```
setmod
```

Selected mixture model: 2 components

| AIC1 |
|------|
| 1 1961.839 |
| 2 1958.803 |
| 3 1962.046 |

Selected spline model degrees of freedom: 2

Knots: -3.958 0.02149 4.001

```
RMSE(nfolds=5, rep=1)
df:1 4.535541
df:2 3.611836
df:3 3.777584
df:4 3.657840
df:5 4.144918
df:6 3.707977
```

Estimate  Std. Error  Z-value  P-value
Measurements:
y1-eta2   1.00000
y2-eta2   0.97794  0.03463  28.24076  <1e-12
y3-eta2   1.04520  0.03473  30.09595  <1e-12
Regressions:
et2-z     1.02819  0.22297  4.61136  4e-06
eta2-eta1_1 3.41773  0.36899  9.26228  <1e-12
eta2-eta2_2 -0.05122  0.00706 -7.25313  <1e-12
Intercepts:
y1        0.00000
```
C.2 Specification of general functional forms

Next, we show how to specify a general functional relation of multiple different latent or exogenous variables. This is achieved via the `predict.fun` argument. To illustrate this we include interactions between the latent variable $\eta_1$ and a dichotomized version of the covariate $z$

```r
# Group variable
d$g <- (d$z<0)*1

# Add grouping variable as exogenous variable (effect specified via 'predict.fun')
mm1 <- regression(m1, -g)

# Add grouping variable as endogenous variable (effect specified via 'predict.fun')
mm2 <- regression(m2, eta2~ u1+u2+u1:g+u2:g+z)

pred <- function(mu,var,data,...) {
  cbind("u1"=mu[,1], "u2"=mu[,1]^2+var[1],
         "u1:g"=mu[,1]*data[,"g"],
         "u2:g"=(mu[,1]^2+var[1])*data[,"g"])
}

ee1 <- twostage(mm1, model2=mm2, data=d, predict.fun=pred)
estimate(ee1,keep="eta2~u",regex=TRUE)
```

| Estimate | Std.Err | 2.5% | 97.5% | P-value |
|----------|---------|------|-------|---------|
| eta2-u1  | 0.9891  | 0.3020 | 0.3971 | 1.5810  | 0.001057 |
| eta2-u2  | -0.3962 | 0.1443 | -0.6791 | -0.1133 | 0.006047 |
| eta2-u1:g | 0.4487  | 0.4620 | -0.4568 | 1.3543  | 0.331409 |
| eta2-u2:g | 0.0441  | 0.2166 | -0.3804 | 0.4686  | 0.838667 |

A formal test show no statistically significant effect of this interaction

```r
summary(estimate(ee1,keep="(:g)", regex=TRUE))
```
Call: estimate.default(x = ee1, keep = "(:g)", regex = TRUE)

| Estimate  | Std.Err  | 2.5%  | 97.5% | P-value |
|-----------|----------|-------|-------|---------|
| eta2-u1:g | 0.4487   | 0.4620| -0.4568| 1.3543  | 0.3314  |
| eta2-u2:g | 0.0441   | 0.2166| -0.3804| 0.4686  | 0.8387  |

Null Hypothesis:
[eta2-u1:g] = 0
[eta2-u2:g] = 0

chisq = 0.9441, df = 2, p-value = 0.6237

C.3 Mixture models

Lastly, we demonstrate how the distributional assumptions of stage 1 model can be relaxed by letting the conditional distribution of the latent variable given covariates follow a Gaussian mixture distribution. The following code explicitly defines the parameter constraints of the model by setting the intercept of the first indicator variable, \(x_1\), to zero and the factor loading parameter of the same variable to one.

```r
m1 <- baptize(m1) ## Label all parameters
intercept(m1, -x1+eta1) <- list(0,NA) ## Set intercept of \(x_1\) to zero.
regression(m1,x1~eta1) <- 1 ## Factor loading fixed to 1
```

The mixture model may then be estimated using the `mixture` method, where the Parameter names shared across the different mixture components given in the `list` will be constrained to be identical in the mixture model. Thus, only the intercept of \(\eta_1\) is allowed to vary between the mixtures.

```r
em0 <- mixture(list(m1,m1), data=d)
```

To decrease the risk of using a local maximizer of the likelihood we can rerun the estimation with different random starting values

```r
em0 <- NULL
ll <- c()
```
for (i in 1:5) {
  set.seed(i)
  em <- mixture(list(m1,m1), data=d, control=list(trace=0))
  ll <- c(ll,logLik(em))
  if (is.null(em0) || logLik(em0)<tail(ll,1))
    em0 <- em
}

summary(em0)

Cluster 1 (n=162, Prior=0.776):

| Measurements:          | Estimate | Std. Error | Z value | Pr(>|z|) |
|------------------------|----------|------------|---------|---------|
| x1-etal                | 1.00000  |            |         |         |
| x2-etal                | 0.99581  | 0.07940    | 12.54101| <1e-12  |
| x3-etal                | 1.06344  | 0.08436    | 12.60542| <1e-12  |
| Regressions:           |          |            |         |         |
| etal-z                 | 1.06675  | 0.08527    | 12.50995| <1e-12  |
| Intercepts:            |          |            |         |         |
| x1                     | 0.00000  |            |         |         |
| x2                     | 0.03845  | 0.09890    | 0.38883 | 0.6974  |
| x3                     | -0.02549 | 0.10333    | -0.24666| 0.8052  |
| etal                   | 0.20923  | 0.13162    | 1.58963 | 0.1119  |
| Residual Variances:    |          |            |         |         |
| x1                     | 0.98539  | 0.13316    | 7.40024 |         |
| x2                     | 0.97181  | 0.13156    | 7.38698 |         |
| x3                     | 1.01316  | 0.14294    | 7.08812 |         |
| etal                   | 0.29047  | 0.11129    | 2.61004 |         |

Cluster 2 (n=38, Prior=0.224):

| Measurements:          | Estimate | Std. Error | Z value | Pr(>|z|) |
|------------------------|----------|------------|---------|---------|
| x1-etal                | 1.00000  |            |         |         |
| x2-etal                | 0.99581  | 0.07940    | 12.54101| <1e-12  |
| x3-etal                | 1.06344  | 0.08436    | 12.60542| <1e-12  |
| Regressions:           |          |            |         |         |
| etal-z                 | 1.06675  | 0.08527    | 12.50995| <1e-12  |
Intercepts:
\[
\begin{align*}
x_1 & : 0.00000 \\
x_2 & : 0.03845 0.09890 0.38883 0.6974 \\
x_3 & : -0.02549 0.10333 -0.24666 0.8052 \\
\eta_1 & : -1.44298 0.25868 -5.57821 2.43e-08
\end{align*}
\]
Residual Variances:
\[
\begin{align*}
x_1 & : 0.98539 0.13316 7.40024 \\
x_2 & : 0.97181 0.13156 7.38698 \\
x_3 & : 1.01316 0.14294 7.08812 \\
\eta_1 & : 0.29047 0.11129 2.61004
\end{align*}
\]
AIC = 1958.803
\[||\text{score}||^2 = 2.124942e-06\]

Measured by AIC there is a slight improvement in the model fit using the mixture model

```r
1 e0 <- estimate(m1, data=d)
2 AIC(e0, em0)
```

df | AIC
---|---
e0 10 | 1961.839
em0 12 | 1958.803

The spline model may then be estimated as before with the \texttt{two-stage} method

```r
1 em2 <- twostage(em0, m2, data=d)
2 em2
```

| Measurements: | Estimate | Std. Error | Z-value | P-value |
|---------------|----------|------------|---------|---------|
| y2-eta2      | 0.97823  | 0.03469    | 28.19903| <1e-12  |
| y3-eta2      | 1.04530  | 0.03484    | 30.00720| <1e-12  |

| Regressions:  | Estimate    | Std. Error    | Z-value   | P-value |
|---------------|-------------|---------------|-----------|---------|
| eta2-z       | 1.02886     | 0.22330       | 4.60763   | 4.073e-06|
| eta2-eta1_1  | 2.80407     | 0.65493       | 4.28149   | 1.856e-05|
| eta2-eta1_2  | -0.02249    | 0.09996       | -0.22495  | 0.822   |
| eta2-eta1_3  | -0.17333    | 0.28933       | -0.59909  | 0.5491  |
|                |        |        |        |        |
|----------------|--------|--------|--------|--------|
| eta2-eta1_4    | 0.38673| 0.33983| 1.13801| 0.2551 |
| Intercepts:    |        |        |        |        |
| y2             | -0.12171| 0.10925| -1.11407| 0.2653 |
| y3             | -0.09870| 0.10546| -0.93592| 0.3493 |
| eta2           | 2.12363| 1.66552| 1.27505| 0.2023 |
| Residual Variances: |        |        |        |        |
| y1             | 1.31872| 0.17657| 7.46862|        |
| y2             | 1.09691| 0.14503| 7.56340|        |
| y3             | 0.81345| 0.13259| 6.13507|        |
| eta2           | 1.99591| 0.28454| 7.01450|        |

In practice the results are very similar to the Gaussian model as shown in Figure ref:fig:mixturefit.

```r
plot(I(eta2-z) ~ eta1, data=d, col=Col("black",0.5), pch=16,
     xlab=expression(eta[1]), ylab=expression(eta[2]))
lines(Estimate ~ eta1, data=as.data.frame(p), col="darkblue", lwd=5)
confband(p[,1], lower=p[,4], upper=p[,5], polygon=TRUE,
         border=NA, col=Col("darkblue",0.2))
pm <- cbind(eta1=newd$eta1,
           estimate(em2, f=function(p) predict(e2,p=p,newdata=newd))$coefmat)
lines(Estimate ~ eta1, data=as.data.frame(pm), col="darkred", lwd=5)
confband(pm[,1], lower=pm[,4], upper=pm[,5], polygon=TRUE,
         border=NA, col=Col("darkred",0.2))
legend("bottomright", c("Gaussian","Mixture"),
       col=c("darkblue","darkred"), lwd=2, bty="n")
```
Figure 8: Model fit with point-wise 95% confidence limits where the measurement model of \( \eta_1 \) is assumed to follow a Gaussian distribution or two-component Gaussian mixture distribution. label:fig:mixturefit
D  Simulation study

In the following we study the structural equation model defined by the stage 1 model:

\[
\xi = \gamma_1 Z + \tilde{\zeta}, \quad Z \sim \mathcal{N}(0, 1), \quad X_{ij} = \xi + \tilde{\epsilon}_j, \quad j = 1, 2, 3
\]  

(36)

and the stage 2 model given by

\[
\eta = \beta^T \varphi(\xi) + \gamma_2 Z + \zeta, \quad Y_j = \eta + \epsilon_j, \quad j = 1, 2, 3
\]

with mutually independent residual terms \(\tilde{\zeta}, \zeta, \tilde{\epsilon}_j, \epsilon_j, j = 1, 2, 3\). The distribution of these terms was varied throughout the simulations. The parameters of primary interest are the structural parameters, \(\beta\), defining the association between the two latent variables \(\xi\) and \(\eta\).

The source code for all the simulations are available in the `twostage` branch of the lava git repository (commit hash: 53e2e18): https://github.com/kkholst/lava/tree/twostage/inst/simulations.

D.1 Corrrectly specified model

We first conducted a simulation study to explore the properties of our estimator in correctly specified models. Data was generated from a quadratic structural model

\[
\eta = \beta_0 + \beta_1 \xi + \beta_2 \xi^2 + \gamma_2 Z + \zeta,
\]

with all residuals \(\tilde{\zeta}_i, \zeta_i, \tilde{\epsilon}_{ij}, \epsilon_{ij}, j = 1, 2, 3\) being standard normal and with \(\beta_0 = 1, \beta_1 = 1, \beta_2 = 0.5\). We compared the 2SSEM estimator (with and with-out mixture model extension) to 2SLS estimation, methods of moments estimation, and approximate ML based on a Laplace approximation as well as Gaussian Adaptive Quadrature with 9 quadrature points. For the mixture 2SSEM estimator we considered only two-component mixtures of the form \(\tilde{\zeta} \sim \pi \mathcal{N}(\mu_1, \sigma^2) + (1 - \pi) \mathcal{N}(\mu_2, \sigma^2)\).
D.1.1 Gaussian model without covariates ($n = 500$)

Here we studied the situation when no covariates were included in neither the data generating model ($\gamma_1 = \gamma_2 = 0$) and the in the estimated models. Sample-size was set to $n = 500$ and all residual terms where normal distributed. See Table 3.

| Method          | Mean  | SD    | SE    | SE/SD | Cov.  | RMSE |
|-----------------|-------|-------|-------|-------|-------|------|
| $\beta_1 = 1$   |       |       |       |       |       |      |
| 2SSEM           | 1.013 | 0.483 | 0.495 | 1.027 | 0.950 | 0.483|
| 2SSEM mixture   | 1.075 | 0.511 | 0.544 | 1.065 | 0.951 | 0.517|
| 2SLS            | 1.031 | 0.978 | 0.893 | 0.913 | 0.940 | 0.978|
| 2SLS robust     | 1.031 | 0.978 | 0.910 | 0.931 | 0.939 | 0.978|
| 2SMM            | 1.108 | 0.623 |       |       | 0.633 |      |
| 2SMM robust     | 1.141 | 0.702 |       |       | 0.716 |      |
| Laplace         | 1.161 | 0.428 | 0.420 | 0.982 | 0.948 | 0.457|
| AGQ9            | 1.030 | 0.382 | 0.390 | 1.023 | 0.956 | 0.383|
| $\beta_2 = 0.5$|       |       |       |       |       |      |
| 2SSEM           | 0.501 | 0.094 | 0.097 | 1.026 | 0.950 | 0.094|
| 2SSEM mixture   | 0.515 | 0.100 | 0.107 | 1.075 | 0.952 | 0.101|
| 2SLS            | 0.507 | 0.173 | 0.147 | 0.851 | 0.920 | 0.173|
| 2SLS robust     | 0.507 | 0.173 | 0.162 | 0.933 | 0.934 | 0.173|
| 2SMM            | 0.520 | 0.116 |       |       | 0.117 |      |
| 2SMM robust     | 0.526 | 0.131 |       |       | 0.133 |      |
| Laplace         | 0.532 | 0.085 | 0.083 | 0.973 | 0.959 | 0.091|
| AGQ9            | 0.506 | 0.075 | 0.076 | 1.013 | 0.951 | 0.075|

Table 3: Simulations from quadratic model without any covariates and Gaussian distribution of all residual terms. Sample-size was $n = 500$ and the number of replications of the simulation study was 1,000.
### D.1.2 Gaussian model without covariates \((n = 1,000)\)

Same setup as in the previous section but with sample size increased to \(n = 1,000\). See Table 4.

| Method          | Mean   | SD     | SE     | \(\frac{SE}{SD}\) | Cov.   | RMSE  |
|-----------------|--------|--------|--------|-------------------|--------|-------|
| 2SSEM           | 0.996  | 0.371  | 0.349  | 0.942             | 0.940  | 0.371 |
| 2SSEM mixture   | 1.031  | 0.393  | 0.424  | 1.079             | 0.941  | 0.394 |
| 2SLS            | 0.975  | 0.647  | 0.606  | 0.938             | 0.938  | 0.647 |
| 2SLS robust     | 0.975  | 0.647  | 0.631  | 0.975             | 0.948  | 0.647 |
| 2SMM            | 1.031  | 0.431  |        | 0.432             |        |       |
| 2SMM robust     | 1.042  | 0.466  |        | 0.468             |        |       |
| Laplace         | 1.127  | 0.306  | 0.292  | 0.957             | 0.939  | 0.331 |
| AGQ9            | 1.002  | 0.277  | 0.272  | 0.984             | 0.947  | 0.277 |

\(\beta_1 = 1\)

| Method          | Mean   | SD     | SE     | \(\frac{SE}{SD}\) | Cov.   | RMSE  |
|-----------------|--------|--------|--------|-------------------|--------|-------|
| 2SSEM           | 0.499  | 0.072  | 0.068  | 0.944             | 0.933  | 0.072 |
| 2SSEM mixture   | 0.507  | 0.077  | 0.084  | 1.095             | 0.934  | 0.077 |
| 2SLS            | 0.496  | 0.115  | 0.100  | 0.864             | 0.919  | 0.115 |
| 2SLS robust     | 0.496  | 0.115  | 0.112  | 0.973             | 0.942  | 0.115 |
| 2SMM            | 0.506  | 0.081  |        | 0.081             |        |       |
| 2SMM robust     | 0.508  | 0.088  |        | 0.088             |        |       |
| Laplace         | 0.526  | 0.060  | 0.057  | 0.958             | 0.939  | 0.065 |
| AGQ9            | 0.501  | 0.054  | 0.053  | 0.986             | 0.943  | 0.054 |

\(\beta_2 = 0.5\)

Table 4: Simulations from quadratic model without any covariates and Gaussian distribution of all residual terms. Sample-size was \(n = 1,000\) and the number of replications of the simulation study was 1,000.
D.1.3 Gaussian model with a covariate \((n = 500)\)

Here we included a covariate \(Z\) in the model with \(\gamma_1 = \gamma_2 = 1\). The sample-size was set to \(n = 500\) and all residual terms where normal distributed. See Table 5. As the methods of moments estimator is not immediately available for estimating models with covariates (Wall and Amemiya, 2000) we omitted it from this simulation.

|            | Mean | SD  | SE  | SE/SD | Cov. | RMSE |
|------------|------|-----|-----|-------|------|------|
| \(\beta_1 = 1\) | 2SSEM | 0.996 | 0.249 | 0.254 | 1.017 | 0.954 | 0.249 |
|            | 2SSEM mixture | 0.991 | 0.248 | 0.256 | 1.029 | 0.956 | 0.249 |
|            | 2SLS | 1.016 | 0.412 | 0.398 | 0.966 | 0.944 | 0.413 |
|            | 2SLS robust | 1.016 | 0.412 | 0.407 | 0.987 | 0.946 | 0.413 |
|            | Laplace | 1.041 | 0.227 | 0.227 | 1.002 | 0.949 | 0.231 |
|            | AGQ9 | 1.000 | 0.219 | 0.222 | 1.010 | 0.945 | 0.219 |

|            | Mean | SD  | SE  | SE/SD | Cov. | RMSE |
|------------|------|-----|-----|-------|------|------|
| \(\beta_2 = 0.5\) | 2SSEM | 0.499 | 0.048 | 0.050 | 1.034 | 0.954 | 0.048 |
|            | 2SSEM mixture | 0.501 | 0.049 | 0.051 | 1.043 | 0.952 | 0.049 |
|            | 2SLS | 0.503 | 0.077 | 0.061 | 0.798 | 0.894 | 0.077 |
|            | 2SLS robust | 0.503 | 0.077 | 0.076 | 0.987 | 0.949 | 0.077 |
|            | Laplace | 0.510 | 0.045 | 0.045 | 0.986 | 0.946 | 0.046 |
|            | AGQ9 | 0.500 | 0.043 | 0.043 | 0.998 | 0.942 | 0.043 |

Table 5: Simulations from quadratic with one covariate \((\gamma_1 = 1, \gamma_2 = 1)\) and Gaussian distribution of all residual terms. Sample-size was \(n = 500\) and the number of replications of the simulation study was 1,000.
D.1.4 Gaussian model with a covariate \((n = 1,000)\)

Same setup as in the previous section but with sample size increased to \(n = 1,000\). See Table 6.

| \(\beta_1 = 1\) | Mean | SD  | SE  | \(\frac{SE}{SD}\) | Cov. | RMSE |
|-----------------|------|-----|-----|------------------|------|------|
| 2SSEM           | 0.997| 0.178| 0.181| 1.017         | 0.950| 0.178|
| 2SSEM mixture   | 0.993| 0.178| 0.182| 1.027         | 0.950| 0.178|
| 2SLS            | 1.000| 0.286| 0.278| 0.973         | 0.940| 0.286|
| 2SLS robust     | 1.000| 0.286| 0.291| 1.019         | 0.951| 0.286|
| Laplace         | 1.039| 0.157| 0.162| 1.026         | 0.958| 0.162|
| AGQ9            | 0.998| 0.151| 0.156| 1.033         | 0.961| 0.151|

| \(\beta_2 = 0.5\) | Mean | SD  | SE  | \(\frac{SE}{SD}\) | Cov. | RMSE |
|-----------------|------|-----|-----|------------------|------|------|
| 2SSEM           | 0.500| 0.035| 0.036| 1.026         | 0.953| 0.035|
| 2SSEM mixture   | 0.501| 0.035| 0.036| 1.040         | 0.950| 0.035|
| 2SLS            | 0.500| 0.054| 0.042| 0.789         | 0.871| 0.054|
| 2SLS robust     | 0.500| 0.054| 0.054| 1.009         | 0.950| 0.054|
| Laplace         | 0.510| 0.031| 0.032| 1.041         | 0.953| 0.032|
| AGQ9            | 0.500| 0.029| 0.030| 1.050         | 0.958| 0.029|

Table 6: Simulations from quadratic with one covariate \((\gamma_1 = 1, \gamma_2 = 1)\) and Gaussian distribution of all residual terms. Sample-size was \(n = 1,000\) and the number of replications of the simulation study was 1,000.
D.1.5 Exponential model

We also assessed the performance of the model with an exponential effect \( \eta = \beta_1 \xi + \beta_2 \exp(\xi) + \zeta \). The consistency of the 2SLS estimator relies on the assumption that the function \( \varphi \) can be decomposed additively as \( \varphi(\xi) = \varphi(x_1 - \tilde{\epsilon}_1) = g_1(x_1) + g_2(x_1, \tilde{\epsilon}_1) \) and with access to instrumental variables (indicators \( X_i \)) that should be uncorrelated with the second term, \( g_2 \). This is not possible with the exponential function, however in a neighbourhood around zero \( \exp(x_1 - \tilde{\epsilon}_1) \approx \exp(x_1) + \exp(x_1)(x_1 - \tilde{\epsilon}_1) \), which suggests a first order approximate 2SLS estimator with \( g_1(x_1) = \exp(x_1) \).

The results of the simulation with an exponential transformation are summarized in Table 7 (\( n = 500 \)). As expected we see that the 2SSEM estimator is unbiased while this is no longer the case for the 2SLS estimator. Also, the coverage of the 2SSEM estimator remains close to the nominal level, however with more extreme choices of the parameters (simulations not shown) we did observe that the sample size needed to be increased to obtain correct coverage levels.

| \( \beta_1 = 0 \) | Mean | SD  | SE  | \( \text{SE/SD} \) | Cov. | RMSE |
|-----------------|------|-----|-----|------------------|------|------|
| 2SSEM           | -0.005 | 0.197 | 0.196 | 0.994          | 0.950 | 0.197 |
| 2SLS            | 0.074  | 0.739 | 0.670 | 0.906          | 0.906 | 0.742 |

| \( \beta_1 = 0.3 \) | Mean | SD  | SE  | \( \text{SE/SD} \) | Cov. | RMSE |
|---------------------|------|-----|-----|------------------|------|------|
| 2SSEM               | 0.303 | 0.173 | 0.172 | 0.997          | 0.905 | 0.173 |
| 2SLS                | 0.151 | 0.398 | 0.342 | 0.859          | 0.698 | 0.425 |

Table 7: Performance of the Gaussian two-stage estimator (2SSEM), under an exponential model, \( \mathbb{E}(\eta | \xi) = \beta_0 + \beta_1 \xi + \beta_2 \exp(\xi) \), with true parameters \( \beta_1 = 0 \) and \( \beta_2 = 0.3 \) where all assumptions hold. The 2SSEM estimator is compared to a first order approximate 2SLS estimator.

D.2 Robustness

Here we explored the properties of the estimators in misspecified models. First we examined data generating mechanisms, where the conditional distribution of the latent variable \( \xi \) was not Gaussian but followed a mixture distribution, i.e.,

\[ \tilde{\zeta} \sim \pi \mathcal{N}(\mu_1, \sigma^2) + (1 - \pi) \mathcal{N}(\mu_2, \sigma^2). \]
The above simulation setup corresponds exactly to the assumptions of our mixture model extension, so to test the robustness of the extension we also included a study where \( \tilde{\zeta} \) followed a uniform distribution with mean zero and variance one, and a simulation where the residuals of the indicators, \( \tilde{\epsilon}_i \) followed a uniform distribution.
D.2.1 Mixture model without covariates \((n = 500)\)

Same as Section D.1.1 with \(\tilde{\zeta}\) following a Gaussian mixture distribution with \(\pi = \frac{1}{4}, \sigma^2 = 1, \mu_1 = 0, \mu_2 = 3\). See Table 8.

| \(\beta_1 = 1\) | Mean | SD  | SE  | \(\text{SE/SD}\) | Cov. | RMSE |
|----------------|------|-----|-----|----------------|------|------|
| 2SSEM          | 1.358| 0.126| 0.123| 0.980          | 0.162| 0.379|
| 2SSEM mixture  | 1.002| 0.148| 0.148| 0.999          | 0.946| 0.148|
| 2SLS           | 1.014| 0.229| 0.280| 1.220          | 0.981| 0.230|
| 2SLS robust    | 1.014| 0.229| 0.231| 1.008          | 0.945| 0.230|
| 2SMM           | 0.998| 0.163|       |                | 0.163|      |
| 2SMM robust    | 0.996| 0.166|       |                | 0.166|      |

| \(\beta_2 = 0.5\) | Mean | SD  | SE  | \(\text{SE/SD}\) | Cov. | RMSE |
|----------------|------|-----|-----|----------------|------|------|
| 2SSEM          | 0.378| 0.041| 0.041| 1.001          | 0.164| 0.129|
| 2SSEM mixture  | 0.499| 0.053| 0.054| 1.023          | 0.948| 0.053|
| 2SLS           | 0.495| 0.076| 0.073| 0.957          | 0.921| 0.077|
| 2SLS robust    | 0.495| 0.076| 0.078| 1.020          | 0.937| 0.077|
| 2SMM           | 0.500| 0.056|       |                | 0.056|      |
| 2SMM robust    | 0.501| 0.058|       |                | 0.058|      |

Table 8: Simulations from quadratic model without any covariates and the latent variable of the stage one model following a Gaussian mixture distribution. Sample-size was \(n = 500\) and the number of replications of the simulation study was 1,000.
D.2.2 Mixture model without covariates ($n = 1,000$)

Same as Section D.1.2 with $\tilde{\zeta}$ following a Gaussian mixture distribution with $\pi = \frac{1}{4}, \sigma^2 = 1, \mu_1 = 0, \mu_2 = 3$. See Table 9.

|                | Mean | SD  | SE  | SE/SD | Cov. | RMSE |
|----------------|------|-----|-----|-------|------|------|
| $\beta_1 = 1$  |      |     |     |       |      |      |
| 2SSEM          | 1.349| 0.088| 0.086| 0.976 | 0.021| 0.360|
| 2SSEM mixture  | 1.000| 0.104| 0.103| 0.988 | 0.948| 0.104|
| 2SLS           | 1.012| 0.169| 0.195| 1.149 | 0.978| 0.170|
| 2SLS robust    | 1.012| 0.169| 0.162| 0.956 | 0.936| 0.170|
| 2SMM           | 1.000| 0.112|       |       | 0.112|      |
| 2SMM robust    | 0.999| 0.114|       |       | 0.114|      |
| $\beta_2 = 0.5$|      |     |     |       |      |      |
| 2SSEM          | 0.380| 0.030| 0.029| 0.976 | 0.025| 0.123|
| 2SSEM mixture  | 0.499| 0.038| 0.038| 0.990 | 0.947| 0.038|
| 2SLS           | 0.496| 0.056| 0.051| 0.903 | 0.915| 0.056|
| 2SLS robust    | 0.496| 0.056| 0.055| 0.976 | 0.929| 0.056|
| 2SMM           | 0.500| 0.040|       |       | 0.040|      |
| 2SMM robust    | 0.500| 0.041|       |       | 0.041|      |

Table 9: Simulations from quadratic model without any covariates and the latent variable of the stage one model following a Gaussian mixture distribution. Sample size was $n = 1,000$ and the number of replications of the simulation study was 1,000.
D.2.3 Mixture model with a covariate \((n = 500)\)

Same as Section D.1.3 with \(\tilde{\zeta}\) following a Gaussian mixture distribution with \(\pi = \frac{1}{4}, \sigma^2 = 1, \mu_1 = 0, \mu_2 = 3\). See Table 10.

| \(\beta_1 = 1\) | Mean | SD  | SE  | \(SE/SD\) | Cov.  | RMSE |
|------------------|------|-----|-----|----------|-------|------|
| 2SSEM            | 1.102| 0.100 | 0.100 | 1.001 | 0.817 | 0.142 |
| 2SSEM mixture    | 1.003| 0.100 | 0.103 | 1.027 | 0.956 | 0.100 |
| 2SLS             | 1.006| 0.167 | 0.199 | 1.193 | 0.977 | 0.167 |
| 2SLS robust      | 1.006| 0.167 | 0.160 | 0.962 | 0.940 | 0.167 |

| \(\beta_2 = 0.5\) | Mean | SD  | SE  | \(SE/SD\) | Cov.  | RMSE |
|-------------------|------|-----|-----|----------|-------|------|
| 2SSEM             | 0.446| 0.034 | 0.033 | 0.974 | 0.599 | 0.064 |
| 2SSEM mixture     | 0.498| 0.037 | 0.037 | 0.992 | 0.943 | 0.037 |
| 2SLS              | 0.497| 0.055 | 0.046 | 0.833 | 0.889 | 0.055 |
| 2SLS robust       | 0.497| 0.055 | 0.053 | 0.961 | 0.929 | 0.055 |

Table 10: Simulations from quadratic with one covariate \((\gamma_1 = 1, \gamma_2 = 1)\) and the latent variable of the stage one model following a Gaussian mixture distribution. Sample-size was \(n = 500\) and the number of replications of the simulation study was 1,000.
D.2.4 Mixture model with a covariate \((n = 1,000)\)

Same as Section D.1.4 with \(\tilde{\zeta}\) following a Gaussian mixture distribution with \(\pi = \frac{1}{4}, \sigma^2 = 1, \mu_1 = 0, \mu_2 = 3\). See Table 11.

| \(\beta_1 = 1\)            | Mean | SD  | SE  | SE/SD | Cov. | RMSE |
|-----------------------------|------|-----|-----|-------|------|------|
| 2SSEM                       | 1.095| 0.072| 0.070| 0.979 | 0.736| 0.119|
| 2SSEM mixture               | 0.997| 0.073| 0.072| 0.994 | 0.940| 0.073|
| 2SLS                        | 1.002| 0.117| 0.140| 1.198 | 0.982| 0.117|
| 2SLS robust                 | 1.002| 0.117| 0.113| 0.968 | 0.933| 0.117|

| \(\beta_2 = 0.5\)          | Mean | SD  | SE  | SE/SD | Cov. | RMSE |
|-----------------------------|------|-----|-----|-------|------|------|
| 2SSEM                       | 0.448| 0.023| 0.023| 1.023 | 0.398| 0.057|
| 2SSEM mixture               | 0.500| 0.025| 0.026| 1.034 | 0.953| 0.025|
| 2SLS                        | 0.498| 0.038| 0.032| 0.846 | 0.896| 0.038|
| 2SLS robust                 | 0.498| 0.038| 0.037| 0.988 | 0.932| 0.038|

Table 11: Simulations from quadratic with one covariate \((\gamma_1 = 1, \gamma_2 = 1)\) and the latent variable of the stage one model following a Gaussian mixture distribution. Sample-size was \(n = 1,000\) and the number of replications of the simulation study was 1,000.
D.2.5 $\tilde{\zeta} \sim U(-\sqrt{\frac{12}{2}}, \sqrt{\frac{12}{2}}) \ (n = 500)$

Same as Section D.1.1 with $\tilde{\zeta}$ following a zero-mean uniform distribution with variance 1. See Table 12.

|                | Mean | SD  | SE  | $\frac{SE}{SD}$ | Cov. | RMSE |
|----------------|------|-----|-----|------------------|------|------|
| 2SSEM          | 0.999| 0.098| 0.098| 0.995           | 0.949| 0.098|
| 2SSEM mixture (2) | 1.000| 0.109| 0.109| 1.005           | 0.944| 0.109|
| 2SSEM mixture (3) | 0.993| 0.107| 0.110| 1.031           | 0.942| 0.107|
| 2SLS           | 1.006| 0.123| 0.121| 0.986           | 0.950| 0.123|
| 2SLS robust    | 1.006| 0.123| 0.128| 1.040           | 0.957| 0.123|
| 2SMM           | 1.005| 0.111|     |                 | 0.111|      |
| 2SMM robust    | 1.005| 0.110|     |                 | 0.110|      |

|                | Mean | SD  | SE  | $\frac{SE}{SD}$ | Cov. | RMSE |
|----------------|------|-----|-----|------------------|------|------|
| 2SSEM          | 0.310| 0.079| 0.079| 1.005           | 0.327| 0.205|
| 2SSEM mixture (2) | 0.493| 0.151| 0.154| 1.016           | 0.932| 0.151|
| 2SSEM mixture (3) | 0.474| 0.145| 0.168| 1.162           | 0.940| 0.147|
| 2SLS           | 0.488| 0.260| 0.228| 0.879           | 0.928| 0.260|
| 2SLS robust    | 0.488| 0.260| 0.242| 0.932           | 0.931| 0.260|
| 2SMM           | 0.555| 0.185|     |                 | 0.193|      |
| 2SMM robust    | 0.541| 0.203|     |                 | 0.207|      |

Table 12: Simulations from quadratic model without any covariates and the latent variable of the stage one model following a uniform distribution. Sample-size was $n = 500$ and the number of replications of the simulation study was 1,000.
D.2.6 $\tilde{\zeta} \sim U(-\frac{\sqrt{12}}{2}, \frac{\sqrt{12}}{2})$ ($n = 1,000$)

Same as Section D.1.2 with $\tilde{\zeta}$ following a zero-mean uniform distribution with variance 1. See Table 13.

|        | Mean | SD  | SE  | SE/SD | Cov. | RMSE |
|--------|------|-----|-----|-------|------|------|
| $\beta_1 = 1$ | 2SSEM | 0.998 | 0.069 | 0.069 | 0.998 | 0.948 | 0.069 |
|        | 2SSEM mixture (2) | 0.998 | 0.075 | 0.075 | 1.007 | 0.957 | 0.075 |
|        | 2SSEM mixture (3) | 0.994 | 0.075 | 0.076 | 1.012 | 0.953 | 0.075 |
|        | 2SLS   | 1.003 | 0.085 | 0.082 | 0.958 | 0.944 | 0.086 |
|        | 2SLS robust | 1.003 | 0.085 | 0.087 | 1.015 | 0.959 | 0.086 |
|        | 2SMM   | 1.001 | 0.078 |       | 0.078 |       |      |
|        | 2SMM robust | 1.001 | 0.077 |       | 0.077 |       |      |
| $\beta_1 = 0.5$ | 2SSEM | 0.310 | 0.054 | 0.056 | 1.030 | 0.102 | 0.198 |
|        | 2SSEM mixture (2) | 0.485 | 0.101 | 0.104 | 1.027 | 0.944 | 0.102 |
|        | 2SSEM mixture (3) | 0.485 | 0.100 | 0.107 | 1.071 | 0.960 | 0.101 |
|        | 2SLS   | 0.489 | 0.160 | 0.149 | 0.930 | 0.923 | 0.161 |
|        | 2SLS robust | 0.489 | 0.160 | 0.159 | 0.994 | 0.934 | 0.161 |
|        | 2SMM   | 0.544 | 0.124 |       |       | 0.131 |
|        | 2SMM robust | 0.520 | 0.126 |       |       | 0.128 |

Table 13: Simulations from quadratic model without any covariates and the latent variable of the stage one model following a uniform distribution. Sample-size was $n = 1,000$ and the number of replications of the simulation study was 1,000.
D.2.7  $\tilde{\epsilon}_j \sim \mathcal{U}(-\frac{\sqrt{12}}{2}, \frac{\sqrt{12}}{2})$ ($n = 500$)

Same as Section D.1.2 with $\tilde{\epsilon}_j, j = 1, 2, 3$ following a zero-mean uniform distribution with variance 1. See Table 14.

|        | Mean | SD  | SE  | SE/SD | Cov. | RMSE |
|--------|------|-----|-----|-------|------|------|
| $\beta_1 = 1$ | 2SSEM | 0.998 | 0.107 | 0.107 | 0.997 | 0.949 | 0.107 |
|        | 2SSEM mixture (2) | 1.002 | 0.117 | 0.118 | 1.012 | 0.942 | 0.117 |
|        | 2SSEM mixture (3) | 0.997 | 0.115 | 0.115 | 0.997 | 0.945 | 0.115 |
|        | 2SLS | 1.003 | 0.138 | 0.116 | 0.844 | 0.915 | 0.138 |
|        | 2SLS robust | 1.003 | 0.138 | 0.131 | 0.951 | 0.953 | 0.138 |
|        | 2SMM | 1.004 | 0.117 | 0.117 | 0.117 | 0.117 |
|        | 2SMM robust | 1.005 | 0.118 | 0.118 | 0.118 |
| $\beta_1 = 0.5$ | 2SSEM | 0.506 | 0.089 | 0.089 | 0.997 | 0.948 | 0.089 |
|        | 2SSEM mixture (2) | 0.527 | 0.106 | 0.108 | 1.018 | 0.961 | 0.109 |
|        | 2SSEM mixture (3) | 0.506 | 0.105 | 0.106 | 1.017 | 0.946 | 0.105 |
|        | 2SLS | 0.498 | 0.131 | 0.102 | 0.781 | 0.873 | 0.131 |
|        | 2SLS robust | 0.498 | 0.131 | 0.124 | 0.944 | 0.909 | 0.131 |
|        | 2SMM | 0.525 | 0.107 | 0.107 | 0.110 | 0.110 |
|        | 2SMM robust | 0.519 | 0.115 | 0.115 | 0.117 |

Table 14: Simulations from quadratic model without any covariates and the residuals of the manifest variables of the stage one model following a uniform distribution. Sample-size was $n = 500$ and the number of replications of the simulation study was 1,000.
D.2.8  \( \tilde{\epsilon}_j \sim \mathcal{U}(-\frac{\sqrt{2}}{2}, \frac{\sqrt{2}}{2}) \) \( (n = 1,000) \)

Same as Section D.1.2 with \( \tilde{\epsilon}_j, j = 1, 2, 3 \) following a zero-mean uniform distribution with variance 1. See Table 15.

| \( \beta_1 = 1 \) | Mean  | SD    | SE    | \( \frac{SE}{SD} \) | Cov. | RMSE |
|------------------|-------|-------|-------|-------------------|------|------|
| 2SSEM            | 0.997 | 0.075 | 0.075 | 1.002             | 0.945| 0.075|
| 2SSEM mixture (2)| 0.998 | 0.082 | 0.082 | 1.000             | 0.935| 0.082|
| 2SSEM mixture (3)| 0.996 | 0.081 | 0.082 | 1.016             | 0.939| 0.081|
| 2SLS             | 0.997 | 0.090 | 0.081 | 0.894             | 0.923| 0.090|
| 2SLS robust      | 0.997 | 0.090 | 0.091 | 1.014             | 0.951| 0.090|
| 2SMM             | 1.000 | 0.079 |       |                   | 0.079|      |
| 2SMM robust      | 1.000 | 0.079 |       |                   | 0.079|      |

| \( \beta_1 = 0.5 \) | Mean  | SD    | SE    | \( \frac{SE}{SD} \) | Cov. | RMSE |
|---------------------|-------|-------|-------|-------------------|------|------|
| 2SSEM              | 0.506 | 0.063 | 0.063 | 0.996             | 0.951| 0.063|
| 2SSEM mixture (2)  | 0.521 | 0.072 | 0.076 | 1.055             | 0.956| 0.075|
| 2SSEM mixture (3)  | 0.511 | 0.072 | 0.076 | 1.065             | 0.957| 0.072|
| 2SLS               | 0.499 | 0.088 | 0.070 | 0.801             | 0.886| 0.088|
| 2SLS robust        | 0.499 | 0.088 | 0.088 | 0.996             | 0.937| 0.088|
| 2SMM               | 0.521 | 0.070 |       |                   | 0.073|      |
| 2SMM robust        | 0.512 | 0.074 |       |                   | 0.074|      |

Table 15: Simulations from quadratic model without any covariates and the residuals of the manifest variables of the stage one model following a uniform distribution. Sample-size was \( n = 1,000 \) and the number of replications of the simulation study was 1,000.
D.3 Larger measurement error

Same as Section D.1.3 with $\tilde{\epsilon}_j, j = 1, 2, 3$ following a zero-mean normal distribution with variance 2. See Table 16. We observe that also in this case with increased measurement error in the stage one model, the $2SSEM$ estimator performs well. Here we also include results on the parameter estimates of the intercepts and covariate effect in the stage two model. Bias in the 2SLS intercept is observed.

|               | Mean   | SD    | SE    | $\frac{SE}{SD}$ | Cov.  | RMSE  |
|---------------|--------|-------|-------|-----------------|-------|-------|
| $\beta_0 = 1$ | 2SSEM  | 1.008 | 0.479 | 0.474           | 0.989 | 0.958 | 0.479 |
|               | 2SSEM mixture | 0.926 | 0.492 | 0.519           | 1.054 | 0.958 | 0.498 |
|               | 2SLS   | 0.024 | 0.784 | 0.966           | 1.232 | 0.860 | 1.252 |
|               | 2SLS robust | 0.024 | 0.784 | 0.780           | 0.995 | 0.719 | 1.252 |
|               | Laplace| 1.253 | 0.392 | 0.390           | 0.996 | 0.922 | 0.466 |
|               | AGQ9   | 0.999 | 0.372 | 0.375           | 1.008 | 0.952 | 0.372 |
| $\beta_z = 1$| 2SSEM  | 0.992 | 0.340 | 0.345           | 1.014 | 0.951 | 0.340 |
|               | 2SSEM mixture | 0.975 | 0.340 | 0.353           | 1.038 | 0.954 | 0.341 |
|               | 2SLS   | 1.017 | 0.711 | 0.695           | 0.978 | 0.951 | 0.711 |
|               | 2SLS robust | 1.017 | 0.711 | 0.690           | 0.971 | 0.946 | 0.711 |
|               | Laplace| 1.059 | 0.291 | 0.289           | 0.994 | 0.956 | 0.297 |
|               | AGQ9   | 0.994 | 0.276 | 0.280           | 1.015 | 0.944 | 0.276 |
| $\beta_1 = 1$| 2SSEM  | 0.992 | 0.340 | 0.345           | 1.014 | 0.951 | 0.340 |
|               | 2SSEM mixture | 0.975 | 0.340 | 0.353           | 1.038 | 0.954 | 0.341 |
|               | 2SLS   | 1.017 | 0.711 | 0.695           | 0.978 | 0.951 | 0.711 |
|               | 2SLS robust | 1.017 | 0.711 | 0.690           | 0.971 | 0.946 | 0.711 |
|               | Laplace| 1.059 | 0.291 | 0.289           | 0.994 | 0.956 | 0.297 |
|               | AGQ9   | 0.994 | 0.276 | 0.280           | 1.015 | 0.944 | 0.276 |
| $\beta_2 = 0.5$| 2SSEM | 0.498 | 0.068 | 0.071           | 1.029 | 0.948 | 0.069 |
|               | 2SSEM mixture | 0.501 | 0.069 | 0.073           | 1.060 | 0.954 | 0.069 |
|               | 2SLS   | 0.503 | 0.132 | 0.109           | 0.822 | 0.893 | 0.132 |
|               | 2SLS robust | 0.503 | 0.132 | 0.128           | 0.970 | 0.937 | 0.132 |
|               | Laplace| 0.511 | 0.060 | 0.059           | 0.977 | 0.946 | 0.061 |
|               | AGQ9   | 0.499 | 0.057 | 0.057           | 1.000 | 0.936 | 0.057 |

Table 16: Simulations from quadratic model with one covariate ($\gamma_1 = 1, \gamma_2 = 1$) and Gaussian distribution of all residual terms. Sample-size was $n = 500$ and the number of replications of the simulation study was 1,000. All residual terms have variance 1 except $\tilde{\epsilon}_j \sim \mathcal{N}(0, 2)$. 
D.4 Non-parametric estimation

To study the estimator in a non-parametric setting we also simulated data from the latent variable model with measurement models as defined in the previous sections but with the unknown functional relationship between the two measurement models given by

$$\phi(\xi; \beta) = \beta_1 \xi + \beta_2 \xi^2 + \sin(\beta_3 \xi)$$

As a benchmark we compared results with the estimator proposed by (Kelava et al., 2017) and the corresponding Matlab implementation\(^2\). Here the number of equidistant spline knots were chosen by dividing the simulated data into a single test and training dataset of equal size and choosing the spline basis (degrees of freedom varying from 1 to 11) as the one that minimized the RMSE evaluated in the test dataset. We noted that slightly better results were obtained for our two-stage estimator when the hyper-parameters (spline knots) were chosen using 5-fold cross validation. To make the results more comparable we, however, adopted the same method for choosing the degrees of freedom for the spline using the exact same split of the testing and training data.

In each simulation, \(r = 1, \ldots, 100\), we simulated \(n = 200\) observations, and for each estimator we calculated

$$\text{RMSE}_r = \left\{ \sum_{i=1}^{n} \left[ \phi(\xi_i; \beta) - \hat{\phi}(\xi_i; \hat{\gamma}_r) \right]^2 \right\}^{1/2},$$

where \(\beta\) denotes the true parameter and \(\hat{\gamma}_r\) is the estimated parameters of the spline model, i.e., \(\hat{\eta} = \hat{\phi}(\xi; \hat{\gamma}_r) = B(\xi)\hat{\gamma}_r\), where \(B(\xi)\) is the spline basis design matrix. See Table 17 and Figure 9 where the estimates are shown from the scenario where \(\beta_1 = 1, \beta_2 = 0, \beta_3 = 1\) and with \(\tilde{\zeta}, \zeta \in \mathcal{N}(0, 1)\).

\(^2\)https://github.com/tifasch/nonparametric/tree/ead709097d6
| $\beta_1$ | $\beta_2$ | $\beta_3$ | $\zeta$ | $\bar{\zeta}$ | RMSE       | Kevala | 2SSEM | 2SSEM-CV(5) |
|----------|----------|----------|--------|--------------|------------|--------|-------|-------------|
| 1        | 0        | 1        | $\mathcal{N}(0, 1)$ | $\mathcal{N}(0, 1)$ | 0.314     | 0.112  | 0.098 |
| 1        | 0        | 1        | $\mathcal{U}(-6, 6)$ | $\mathcal{U}(-6, 6)$ | 0.933     | 0.608  | 0.585 |
| 1        | 0        | 1        | $\mathcal{G}(4, 4, 0.5)$ | $\mathcal{N}(0, 1)$ | 0.200     | 0.143  | 0.101 |
| 0        | 1        | 3        | $\mathcal{N}(0, 1)$ | $\mathcal{N}(0, 1)$ | 1.177     | 0.827  | 0.625 |
| 0        | 1        | 3        | $\mathcal{U}(-6, 6)$ | $\mathcal{U}(-6, 6)$ | 3.614     | 1.988  | 1.860 |
| 0        | 1        | 3        | $\mathcal{G}(4, 4, 0.5)$ | $\mathcal{N}(0, 1)$ | 6.322     | 1.658  | 1.590 |

Table 17: Comparison of the 2SMM estimator and the estimation procedure of Kelava et al. (2017).
Figure 9: Comparison of the two-stage estimator and the estimation procedure of Kelava et al. (2017). The dashed red line is the true association between $\xi$ and $\eta$ and the dotted blue line is the average estimated association over the 100 replications. The transparent lines show the estimated spline for each of the replications.