14

MODELING CHANGE WITH DATA COLLECTED FROM RELATIVES[1]

Michael C. Neale

PROOF

Introduction

I first met Jack McArdle in the cafeteria of the Institute of Psychiatry at King's College in London, when I was a graduate student with David Fulker. Jack had visited in part to discuss modeling of data from twins and their parents, which was to become a central part of my PhD thesis. We considered a path diagram of genetic and cultural transmission from parents to their twin children, to which Jack added an auto-correlation path to represent residual variation in the child's genotype. This tweak to the diagram seemed rather trivial and insignificant at the time; Fulker and I exchanged skeptical glances and may have smirked a bit. Jack was in fact giving us a lesson in precise specification of a structural equation model via a mathematically complete path diagram. Little did I realize that I was going to become one of its most ardent devotees. It took some years, and my move to the United States before I fully understood the value of a mathematically complete path diagram of a structural equation model. Early in the 1990s, while actively collaborating with Jack, I developed the program Mx (Neale, 1991). Its graphical interface, with which users could directly specify and fit models to data, would not have existed without the influence of McArdle on myself and our mutual friend and colleague Steve Boker. Today, the same method underwrites graphical modeling software such as Onyx (von Oertzen, Brandmaier, & Tsang, 2017) or Amos (Arbuckle, 1995). In practice, diagram-based modeling is a valuable teaching tool, and useful for small- to medium-sized models. Larger models are usually more efficiently programmed via matrix algebra or purpose-built functions that specify the data, model type and optimizer or other options.

Assortative Mating

My first publication with Jack concerned resemblance between spouses (Neale & McArdle, 1990), which can arise from assortative mating, i.e., like marrying like. Marital resemblance is weak or absent for many personality traits, but is very substantial for educational attainment, political affiliation, and substance use. It is significant in genetic epidemiology because the genotypes of the parents become correlated, which in turn increases the genetic variance and covariances between siblings in the next generation. We had figured out a way to represent the assortative mating model in LISREL (Joreskog & Sorbom, 1996) and published it. The model involved multivariate path analysis (Vogler, 1985), in which each variable in a path diagram may represent a vector of (latent or observed) variables, and the paths between them consist of matrices. Subsequently, we experimented with specifying the model with the RAMPATH software he co-developed with Steve Boker. The software found a simpler drawing that avoided paths crossing as they do in Figure 14.1 of the 1990 paper. These diagrams are shown in Figure 14.1. My original diagram was drawn with the idea of keeping all the husbands' variables on one side of the figure, and all the wives' variables on the other. However, it had the disadvantage that two paths crossed each other; RAMPATH's automatic drawing avoided this intersection. Being taught such simple things by a computer program can be rewarding for any user; for developers there is the additional sense of completing the circle one began by teaching the computer to do new things.

Psychometric and Biometric Factor Models

Data collected from relatives such as monozygotic (MZ) and dizygotic (DZ) twins permit partitioning of trait variation into components associated with genetic and environmental factors. The value of this natural experiment was appreciated in the nineteen century by Sir Francis Galton (1875), and the comparison of MZ and DZ pairs' similarities was developed by Merriman (1924). However, despite the development of path analysis by Sewall Wright (1921) many years would pass before structural equation modeling software capable of fitting models simultaneously to multiple groups would be developed and it was not until the 1990s that SEM became the method of choice for analyzing data from twins and other relatives.

McArdle and Goldsmith (1990) recognized that multivariate data from twins could be analyzed by extending a factor model in two ways. The "Psychometric Factor" model (a.k.a. the Common Pathway model) takes the usual single factor model and partitions all the latent variables (i.e., the random effects) into additive genetic (A), common environment (C; shared by twins) and non-shared environment (E) components. Figure 14.2 shows a path diagram of this model when there are three orthogonal factors: F1, F2, and F3. A popular alternative to this model is to impose restrictions such that the latent factors'

"Chapter14" — 2018/7/13 — 18:30 — page 303 — #3

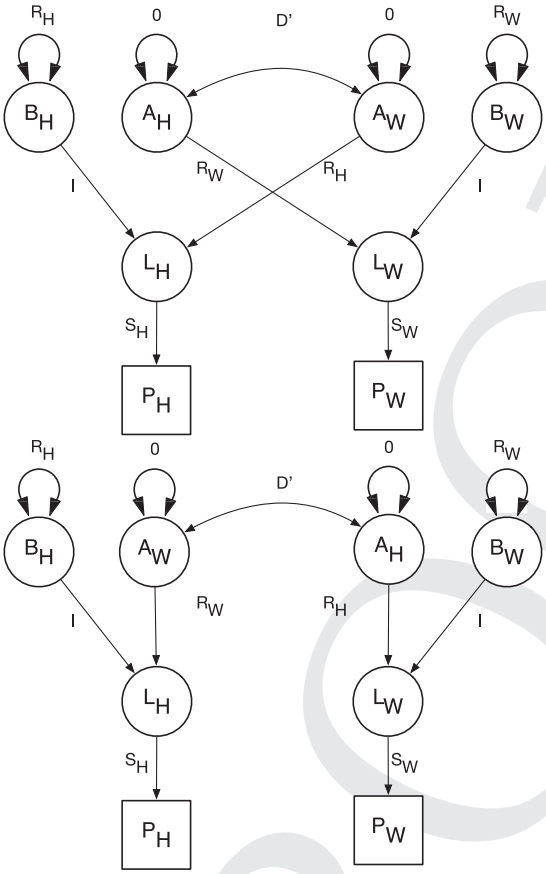

FIGURE 14.1 Multivariate path diagrams for modeling marital resemblance for multiple traits. Left: diagram designed by human being (MCN); Right: diagram designed by intelligent software (RAMPATH). The zero variance-covariance matrices atop the A_H and A_W variables generate covariance between spouses' phenotypes (P_H and P_W), but do not affect their variances.

variance is assumed to be composed of entirely one type of variation, A, C, or E. This second 'Biometric Factor' model (a.k.a. the Independent Pathway model) is shown in Figure 14.3; it has six fewer free parameters than the three-factor psychometric model. To identify the model, the latent factor variances are typically constrained to equal unity, so effectively the models differ by just three unconstrained parameters. Many applications of these two models have sadly compared only the single psychometric factor model (Figure 14.2 without F2 or F3), to the three-factor biometric one, and found the latter to fit much better. Those with experience in analyses of unrelated persons will divine that a single factor model often fits worse than a three-factor one, and that exactly the same type of data are represented in the within-person covariances of the individual twins. Failure to specify enough within-person factors is poor rationale

PROOF

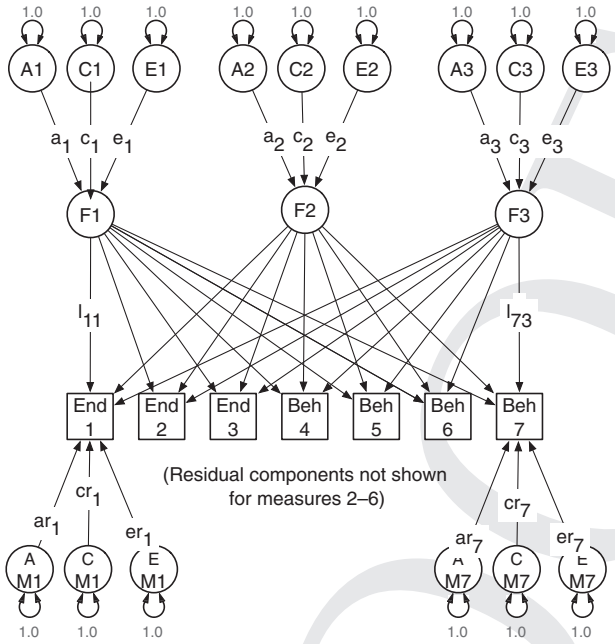

FIGURE 14.2 Psychometric factor model for data collected from twins or other relatives. Latent factors F1, F2, and F3 influence seven measured variables M1–M7. Variation in the latent factor and the residual, variable-specific components are partitioned into additive genetic, shared and unique environment components (A, C, and E, respectively). Model identification requires two types of relative, with differences in the degree of covariation between the relatives' A and C variance components.

to favor the biometric factor model over the single-factor psychometric one. A reviewer requested examples of this pattern, of which there are many in *Behavior Genetics* and similar journals. It seems best to identify a few publications that I myself co-authored before realizing the oversight (Kendler, Neale, Kesslier, Heath, & Eaves, 1992; Kendler, Walters, Neale, KIesslier, Heath, & Eaves, 1995). Indeed, I seemed to be comfortable with that approach in Kendler (1995), in which we stated "the common pathway model was rejected, suggesting that the genetic and environmental risk factors for these disorders are not influencing comorbidity in the same manner." (Kendler, Walters, Neale, Kessler, Heath, & Eaves, 1995). While that conclusion may be correct, fitting "the" common pathway model (as if there is only one, the single factor variety) is insufficient for it to be drawn. Here I note that both types of model may be extended by adding either psychometric or biometric factors, and that this could be done *ex hypothesi* for confirmatory work, or automatically using, for example, a loop in R. The resulting long list of models might be summarized by model-averaging. However, it is the opinion of this author that the biometric factor model is intrinsically less plausible for most (and perhaps all) complex

PROOF

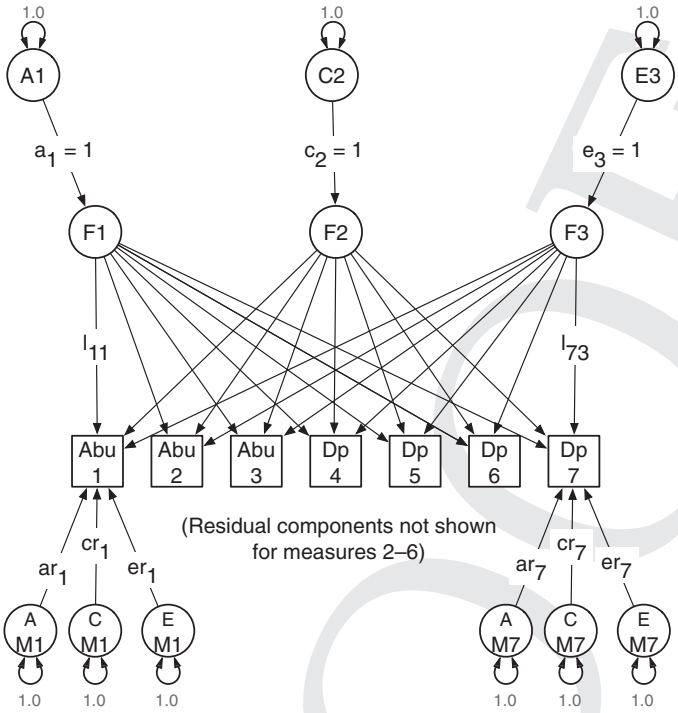

FIGURE 14.3 Biometric factor model for data collected from twins or other relatives. Latent factors F1, F2, and F3 influence seven measured variables M1–M7. Variation in latent factor F1 is specified as entirely additive genetic, that in F2 is entirely common environment, and F3 is exclusively unique environment. Model identification requires two types of relative, with differences in the degree of covariation between the relatives' A and C variance components.

behavioral traits. Genetic and environmental influences seem likely to act together on the structure and function of the brain or other physiological systems en route to affecting variation in behavioral and psychological traits. That is, so-called endophenotypes – such as size or connectivity of brain regions – likely combine genetic and environmental influences during their development prior to affecting, e.g., psychiatric, psychological, and behavioral traits that are often the primary outcomes of interest (Meyer-Lindenberg & Weinberger, 2006). Therefore, McArdle's psychometric factor model seems optimal for this area of research – with more than one factor if the data so warrant. This is an empirical question that was not often addressed in the past; I hope that future analyses will do so.

Latent Growth Modeling

Dr McArdle has also made great contributions to the genetic modeling of longitudinal, repeated measures data. He is credited with adapting growth curve models such as that of Meredith and Tisak (1984) and Browne (1993) for

application to data with twins. His 1986 paper partitioned latent factors into A and E components alone, although there was no impediment to including shared environmental variance components McArdle, (1986). Similarly, with Aki Hamagami, he added biometric components to latent change score models (MArdle & Hamagami, 2003), enabling dynamical systems perspective on genetic and environmental factors in development. Here I focus on the latent growth curve approach, on which he and I collaborated to develop in the early 1990s, although it was not until the turn of the century that these methods were finally published. To publish original material some six years later than planned is a luxury afforded to those, such as Jack, who are many years ahead of the field.

Most latent growth curve (LGC) models use two or more factors to represent level, linear (and possibly quadratic or other) growth by fixing the factor loadings to particular values. McArdle initially followed the Meredith and Tisak approach, in which some factor loadings were estimated as free parameters. Since then, growth curve factors have, with rare exception, used the fixed factor loadings approach; loadings for the level factor are all set to 1.0, those for the linear growth factor are set to increasing integers (0, 1, 2…), and those for the quadratic are the square of the linear. This polynomial approach is suitable for growth processes about which we have little knowledge or theory to guide curve type selection. Although the polynomial model may provide a good fit to data over a limited developmental period, it is often poor when the measurement window is extended. This is true, even of the less widely-applied growth curve models that include quadratic components: asymptotic behavior is difficult to approximate with a small number of polynomial factors. Human height, for example, follows two periods of accelerated development, which the Preece-Baines curve closely models (Beunen, Thomis, Maes, Loos, Malina, Claessens, & Vlietinck, 2000), with asymptotic behavior that matches the leveling off of human height in adulthood. Accordingly, I now consider factor modeling of growth with particular functional forms, i.e., a parametric growth curve (PGC) approach.

In our 2000 paper, McArdle and I showed how Gompertz, Logistic and Exponential family curves could be specified and fitted to data from MZ and DZ twin pairs (Neals & McArdle, 2000). Fitting such growth curves seems rational for many ongoing studies. For example, the Adolescent Behavioral and Cognitive Development (ABCD, 2017) study, which is currently collecting longitudinal data on brain development and cognition from 11,500 9 to 10-year-old youths, including 800 pairs of twins. This is but one example of Jack's contributions to the study of development, which will surely benefit research studies long into the future. The 2000 treatment used classic Mx (Neale, Bokrer, Xie, & Maes, 2003) to fit models to summary statistics consisting of means and covariance matrices, but this software is no longer supported since it was superseded by OpenMx (Boker, Neale, Maes, Wilde, Spiegel, Brick, Spies, Estabrook, Kenny, Bstes, Mehta, & Fox, 2011); Neale, Hunter, Pritikin, Zahery, Brick, Kirkpatrick, Estabrook, Bates, Maes, & Boker, (2016). Endel Tulving remarked "a Festschrift frequently enough also serves as a convenient place in which those who are invited to contribute find

a permanent resting place for their otherwise unpublishable or at least difficult-to-publish papers" (Tulving, 2007). It therefore seems appropriate to revisit the growth curve models of the 2000 paper, using modern analytical methods. Open source software increases reliability and reproducibility of findings, and safeguards its legacy, so implementation in OpenMx seems worthwhile. Here we have an opportunity to self-examine; if the original researcher cannot reproduce their own results, it seems unlikely that others would.

Modeling growth curves such as those that arise from differential equations is a more complex task than is usual for structural equation modeling. Effectively, the factor loadings are neither constants nor free parameters, but complex functions obtained as the partial derivatives of the growth curve function with respect to its free parameters. The expected means are obtained directly from the growth curve function itself, but these too may involve non-trivial algebra. In our 2000 paper, Jack and I tabulated these derivatives for the Logistic, Gompertz and Exponential growth curve forms (Neale & McArdle, 2000). Here, for illustration, I reproduce the equations for the Gompertz curve in Table 14.1. Figures 14.4 and 14.5 respectively show path diagrams for the conventional level, slope, and quadratic polynomial component LGC model, and a parametric structured curve model. The primary difference between the figures is that in the LGC model the factor loadings are fixed to constant values, whereas in the PGC model the loadings are complicated algebraic functions of the free parameters of the growth curve being fitted.

Some interesting things happened in the attempted reproduction of the results using OpenMx instead of classic Mx. Translating the script was straightforward, but the original data files could not be found. The covariance matrices and means were, however, published in Jack's 1986 paper, so they were re-entered (McArdle, 1986). Fitting the models anew, the results were similar but not identical to those of the original article. The number of estimated parameters were the same in OpenMx and classic, but the chi-squared fit of all the models had deteriorated by some 20 units. To identify the source of this issue, the models were refitted using the Mx version 1.69, which generated very similar values for model fit and parameter estimates to those obtained by OpenMx. This agreement increased once the sample sizes for Mx were increased from 75 to 76, because OpenMx's fit function uses N rather than N-1 when fitting to summary statistics, to be consistent with its full information maximum likelihood fit function. With one exception, the remaining differences in model fit between OpenMx and Mx were less than a single unit of chi-squared, and likely due to differences in numerical precision and orders of operation when evaluating the log-likelihood. Optimization can be sensitive to relatively slight changes in numerical precision, although both programs appear satisfied that they have arrived at a strong local, and possibly global minimum. The single exception is that the effect of dropping all the occasion-specific familial components, A_s and C_s, is approximately 4.6 chi-squared units greater with Mx than with OpenMx. This appears to be an

PROOF

TABLE 14.1 Parametric growth curve functions F_x for Gompertz ($x = G$), Exponential ($x = E$) and Logistic ($x = L$) curves, and their partial derivatives $\frac{dF_x}{d\theta}$ with respect to the elements of the free parameter vector θ for asymptote (a), initial (i), and rate (r), as a function of time t. The partial derivative vectors for $t = 1 \ldots T$ are used as the factor loadings (e.g., dy/da) shown in Figure 14.5. Further details are given in Neale and McArdle (2000), on which this table was based.

Gompertz

$$F_G = a\exp\left[\log[\frac{i}{a}]\exp[-(t-1)r]\right] \quad (14.1)$$

$$\frac{dF_G}{da} = [1-\exp[-(t-1)r]]\exp\left[\log[\frac{i}{a}]\exp[-(t-1)r]\right] \quad (14.2)$$

$$\frac{dF_G}{di} = \frac{a}{i}\exp\left[-(t-1)r+\log[\frac{i}{a}]\exp[-(t-1)r]\right] \quad (14.3)$$

$$\frac{dF_G}{dr} = -a\log[\frac{i}{a}](t-1)\exp\left[-(t-1)r+\log[\frac{i}{a}]\exp[-(t-1)r]\right] \quad (14.4)$$

Exponential

$$F_E = a-(a-i)\exp[-(t-1)r] \quad (14.5)$$

$$\frac{dF_E}{da} = 1-\exp[-(t-1)r] \quad (14.6)$$

$$\frac{dF_E}{di} = \exp[-(t-1)r] \quad (14.7)$$

$$\frac{dF_E}{dr} = (a-i)(t-1)\exp[-(t-1)r] \quad (14.8)$$

Logistic

$$F_L = \frac{ai}{i+(a-i)\exp[-(t-1)r]} \quad (14.9)$$

$$\frac{dF_L}{da} = \frac{i-\exp[-(t-1)r]F_L}{i+(a-i)\exp[-(t-1)r]} \quad (14.10)$$

$$\frac{dF_L}{di} = \frac{a-\left(1-\exp[-(t-1)r]\right)F_L}{i+(a-i)\exp[-(t-1)r]} \quad (14.11)$$

$$\frac{dF_L}{dr} = \frac{(a-i)(t-1)\exp[-(t-1)r]F_L}{i+(a-i)\exp[-(t-1)r]} \quad (14.12)$$

optimization failure on behalf of the older software, possibly due to the order in which the models were fitted. Eliminating variance components that account for a substantial proportion of variance can make for poor starting values for subsequent model fitting attempts, a general point to be aware of when using model-fitting software.

PROOF

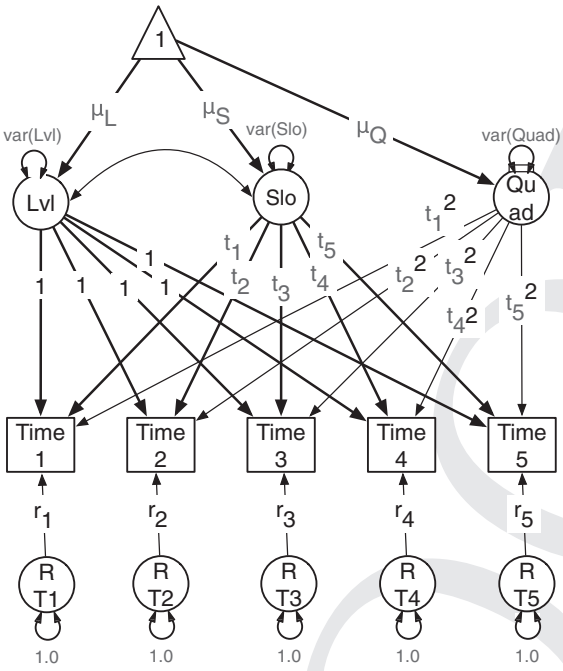

FIGURE 14.4 Latent Growth Curve Model with Level (Lvl), Slope (Slo) and Quadratic (Quad) variance components. These factors have means $\mu_L, \mu_S and \mu_Q$. Typically, values of the factor loadings $t_1, t_2 \ldots t_5$ are fixed to integer values such as $1, 2 \ldots 5$. In practice, individuals may differ with respect to age at assessment, and may be substituted with individuals' ages at measurement on a casewise basis using, e.g., definition variables in OpenMx.

Table 14.2 shows parameter estimates from fitting the logistic, exponential, and Gompertz growth curves to the Bayley Infant Mental Development data, in the same format as Table 14.2 in Neale and McArdle (2000). Goodness-of-fit statistics of the three models and a set of seven submodels are shown in Table 14.3. The bad news is that neither the goodness-of-fit statistics nor the parameter estimates agree 100% with those from the original article. However, the main substantive conclusions have **not** changed; much of the variation in the random components of the growth curves is associated with shared environmental factors, there remains substantial (residual) variation not associated with the growth curve factors, and some of the residual, time-specific variation is shared between the members of the twin pair. The origin of the disparities between this description and that of Neale and McArdle (2000) seems to be the data files; using the new data shows close, but not perfect agreement between classic Mx and its successor. A further point to note is that the sample size and number of occasions of measurement are both relatively small for the intended purpose of estimating latent growth curves. These limitations make optimization more difficult, because the fit function may change

PROOF

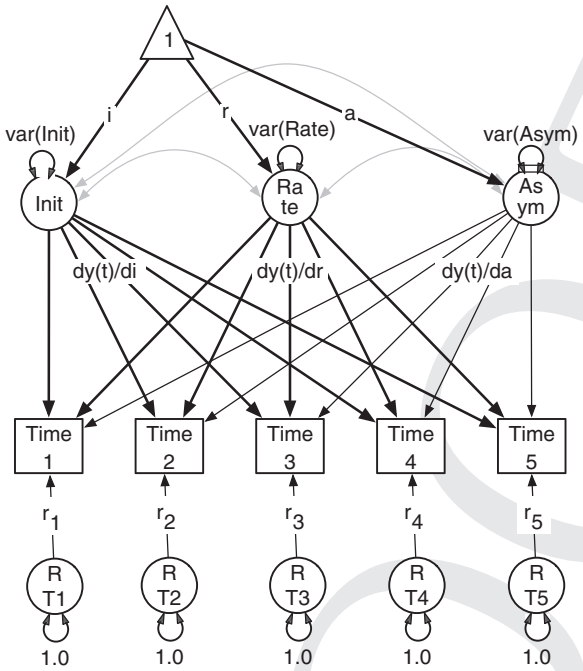

FIGURE 14.5 Structural Model for Functional Latent Growth Curves featuring asymptote (*A*), initial (*I*), and rate (*R*) variance components, which generate variation in the observed measures on occasions (Time 1 . . . 5. The factor loadings denoted, e.g., $dy(t)/di$, are partial derivatives of the growth curve function with respect to its initial (*i*), rate (*r*) and asymptote (*a*) parameters; these parameters are also the estimated means of the latent factors.

little in response to a change in parameter value, i.e., the gradients, being the partial derivatives of the fit function with respect to the parameters are almost flat.

The scripts and data files used in this article can be found on the following website: http://somewhere.suggested.by.editor?. These, we hope, will facilitate future uses of the method of fitting structured latent growth curves to data from relatives. The scripts can also be used to fit models to data from unrelated persons, but the genetic and shared environmental variance components at both the factor and residual levels should be set to zero. In effect, the model becomes one of random, individual-specific effects, which, to a behavioral geneticist, seems a strong assumption. It is important for researchers from all disciplines to recognize that variance components at both the factor and occasion-specific (residual) levels may include reliable and familial components of variance.

Conclusions

This chapter embarked on a reproducibility exercise, using entirely different software (to create OpenMx no code was 'borrowed' from Mx – all code was

TABLE 14.2 Parameter estimates for three growth curve models fitted to Bayley Infant Mental Development data on MZ and DZ twins assessed at four occasions. Variance in the growth curve components a, i, and r due to genetic (G_f), common environment (C_f) and specific environment (E_f) factors are shown on the diagonal of matrices, with covariances below and correlations above. Variance due to occasion-specific genetic and environmental factors A_s, C_s, and E_s are shown for the four occasions t_1 to t_4.

Parameter	*Model*											
	Exponential				*Logistic*				*Gompertz*			
a				116.98				84.75				93.64
i				39.90				40.11				39.99
r				0.11				0.37				0.24
		a	i	r		a	i	r		a	i	r
Gf	a	528.48	−18.85	−1.14	a	5.21	−2.05	−0.11	a	43.08	−5.61	−0.32
	i	−18.85	0.67	0.04	i	−2.05	0.80	0.04	i	−5.61	0.73	0.04
	r	−1.14	0.04	0.00	r	−0.11	0.04	0.00	r	−0.32	0.04	0.00
		a	i	r		a	i	r		a	i	r
Cf	a	6726.92	−49.58	−9.70	a	382.38	−5.37	−1.17	a	1013.65	−13.34	−2.84
	i	−49.58	10.25	0.07	i	−5.37	9.85	−0.03	i	−13.34	10.05	0.02
	r	−9.70	0.07	0.01	r	−1.17	−0.03	0.00	r	−2.84	0.02	0.01
		a	i	r		a	i	r		a	i	r
Ef	a	1035.26	20.57	−1.63	a	77.61	5.51	−0.40	a	180.93	8.51	−0.65
	i	20.57	0.41	−0.03	i	5.51	0.39	−0.03	i	8.51	0.40	−0.03
	r	−1.63	−0.03	0.00	r	−0.40	−0.03	0.00	r	−0.65	−0.03	0.00
	t_1	t_2	t_3	t_4	t_1	t_2	t_3	t_4	t_1	t_2	t_3	t_4
A_s	2.31	1.28	2.12	0.00	2.33	1.24	2.11	0.00	2.31	1.28	2.12	0.00
C_s	1.03	0.00	0.00	0.00	1.06	0.00	0.25	0.00	1.05	0.00	0.00	0.00
E_s	2.04	1.96	1.80	1.91	2.04	1.95	1.80	1.89	2.04	1.96	1.80	1.90

PROOF

"Chapter14" — 2018/7/13 — 18:30 — page 311 — #11

TABLE 14.3 Fit statistics obtained for Growth curve models and submodels applied to Bayley Infant Mental Development data on MZ and DZ twins.

	Fit Statistic			*Difference* χ^2		
Model	χ^2	*d.f.*	*AIC*	χ^2	*d.f.*	*p*
			Exponential			
Full	148.90	55	38.90	—	—	—
Orthogonal	163.28	64	35.28	14.38	9	0.11
No A	157.37	61	35.37	8.47	6	0.21
No C	190.86	61	68.86	41.96	6	0.00
No E	159.86	61	37.86	10.96	6	0.09
No A_s,C_s	187.72	63	61.72	38.82	8	0.00
No A_s	158.44	59	40.44	9.54	4	0.05
No C_s	149.02	59	31.02	0.12	4	1.00
			Logistic			
Full	157.55	55	47.55	—	—	—
Orthogonal	168.54	64	40.54	10.99	9	0.28
No A	165.58	61	43.58	8.03	6	0.24
No C	198.63	61	76.63	41.08	6	0.00
No E	168.39	61	46.39	10.84	6	0.09
No A_s, C_s	202.17	63	76.17	44.62	8	0.00
No A_s	167.20	59	49.20	9.65	4	0.05
No C_s	157.70	59	39.70	0.15	4	1.00
			Gompertz			
Full	151.88	55	41.88	—	—	—
Orthogonal	164.46	64	36.46	12.58	9	0.18
No A	160.17	61	38.17	8.29	6	0.22
No C	193.45	61	71.45	41.57	6	0.00
No E	162.78	61	40.78	10.91	6	0.09
No A_s, C_s	192.77	63	66.77	40.89	8	0.00
No A_s	161.38	59	43.38	9.51	4	0.05
No C_s	152.01	59	34.01	0.14	4	1.00

freshly developed). Encouragingly, only modest differences were found between the two implementations of extended structural equation modeling, and no change in substantive conclusions was warranted. The one exception shows better optimization performance with OpenMx than with Mx, which indicates progress. It should be noted that OpenMx offers several different optimization algorithms – with more planned for future releases – although the same optimizer, NPSOL (Gill, Murray, Saunders, & Wright, 1986), was used in both packages for this illustration.

Finally, I have tremendous respect for Professor McArdle and his many contributions to behavioral science generally, and to multivariate and developmental behavioral genetics in particular. His influence on my own career was quite profound. In the early days of developing Mx, Jack recommended that I

PROOF

not join others who were selling their structural equation modeling software. This advice proved crucial; I have not had to trouble myself with running a business as well as a research team at VCU. I also feel that having obtained tax payer money to develop the software, it would be immoral to charge users for purchase or license fees, because the same tax payer would likely have to foot the bill for them. Indeed, Jack's insight foreshadowed the rise of open source software and open science – principles with which I whole-heartedly agree. For science, anything other than open source software should be considered unfit for purpose. One approach to validating a model-fitting program is to feed it data simulated using known parameter values to see if its parameter estimates do not depart from them for reasons other than sampling error. However, this method is analogous to a Turing test for artificial vs. human intelligence. The concept is to feed questions in through a letterbox, on the other side of which is either a human or a machine, which responds without directly revealing its mechanism. With a series of such questions, a Turing test may establish with some degree of confidence whether the room contains a human being or a computer. This confidence is typically much less than would be obtained if one could look inside the room and examine its contents. Open source software puts the researcher in the position of being able to examine the contents of the room. Indeed, a user of closed source software should really run simulation tests on every model being used, to ensure that no "corner case" bug exists. Even then, the best that can be achieved outside the black box is support for the hypothesis that it is doing the right thing. While keeping the source code secret may be good from the perspective of maintaining an economic advantage over one's competitors, it seems poor for the purposes of reproducible scientific research. Structural equation modeling, and especially the field of behavioral genetics, are indebted to Dr McArdle for his prescient wisdom in recommending free and open source software for scientific research.

Note

1 This study was supported by NIDA grants R01DA-018673 and R25DA-26119.

References

ABCD (2017). The adolescent study of cognitive development http://abcdstudy.org. Technical report, University of San Diego, http://abcdstudy.org

Arbuckle, J. L. (1995). *AMOS for Windows. Analysis of moment structures (Version 3.5)*. Chicago, IL: SmallWaters.

Beunen, G, Thomis, M., Maes, H. H., Loos, R., Malina, R. M., Claessens, A. L., & Vlietinck, R. (2000). Genetic variance of adolescent growth in stature. *Annals of Human Biology*, *27*(2), 173–186.

Baker, S., Neale, M., Maes, H. H., Wilde, M., Spiegel, M., Brick, T. R., Spies, J., Estabrook, R., Kenny, S., Bates, T., Mehta, P., & Fox J. (2011). OpenMx: An open source extended structural equation modeling framework. *Psychometrika*, *76*(2), 306–11.

PROOF

Browne, M. W. (1993). Structured latent curve models. In C M Cuadras and C R Rao, editors, *Multivariate analysis: Future directions 2*, pages 171–198. Amsterdam: North-Holland Publishing Co.

Galton, F. (1875). The history of twins, as a criterion of the relative powers of nature and nurture. *Fraser's Magazine*, *12*: (pp. 566–576).

Gill, P. E., Murray, W., Saunders, M. A., and Wright, M. H. (1986). User's guide for npsol (version 4.0): A FORTRAN package for nonlinear programming. Technical Report SOL 86–2, Department of Operations Research, Stanford University, Stanford.

Jöreskog, K. G. and Sörbom, D. (1996). *LISREL 8 User's Reference Guide*. Mooresville, IN: Scientific Software, Inc.

Kendler, K. S., Neale, M. C., Kessler, R. C., Heath, A. C., and Eaves, L. J. (1992). The genetic epidemiology of phobias in women. the interrelationship of agoraphobia, social phobia, situational phobia, and simple phobia. *Arch Gen Psychiatry*, *49*(4), 273–81.

Kendler, K. S., Walters, E. E., Neale, M. C., Kessler, R. C., Heath, A. C., & Eaves, L. J. (1995). The structure of the genetic and environmental risk factors for six major psychiatric disorders in women. phobia, generalized anxiety disorder, panic disorder, bulimia, major depression, and alcoholism. *Arch Gen Psychiatry*, *52*(5), 374–83.

McArdle, J. J. (1986). Latent variable growth within behavior genetic models. *Behavioral Genetics*, *16*(1), 163–200.

McArdle, J. J. & Goldsmith, H. H. (1990). Alternative common-factor models for multivariate biometric analyses. *Behavioral Genetics*, *20*, 569–608.

McArdle, J. J. & Hamagami, F. (2003). Structural equation models for evaluating dynamic concepts within longitudinal twin analyses. *Behavioral Genetics*, *33*(2), 137–159.

Meredith, W. & Tisak, J. (1984). Tuckerizing curves. *Paper presented at Psychometric Society Annual Meeting, Santa Barbara CA*.

Merriman, C. (1924). The intellectual resemblance of twins. *Psychological Monographs*, *33*, 1–58.

Meyer-Lindenberg, A. & Weinberger, D. R. (2006). Intermediate phenotypes and genetic mechanisms of psychiatric disorders. *Nat Rev Neurosci*, 7(10), 818–27.

Neale, M. C. (1991). *Mx: Statistical Modeling*. Box 710 MCV, Richmond, VA 23298: Department of Human Genetics.

Neale, M. C. & McArdle, J. J. (1990). The analysis of assortative mating: a lisrel model. *Behavioral Genetics*, *20*(2), 287–96.

Neale, M. C. & McArdle, J. J. (2000). Structured latent growth curves for twin data. *Twin Research*, *3*, 165–77.

Neale, M. C., Boker, S. M., Xie, G., & Maes, H. H. (2003). *Mx: Statistical Modeling*. Department of Psychiatry, Virginia Commonwealth University, Box 980126 Richmond VA, 6th edition.

Neale, M. C., Hunter, M. D., Pritikin, J. N., Zahery, M., Brick, T. R., Kirkpatrick, R. M., Estabrook, R., Bates, T. C., Maes, H. H. M., & Boker, S. M. (2016). OpenMx 2.0: Extended structural equation and statistical modeling. *Psychometrika*, *81*(2), 535–49.

Tulving, E. (2007). Are there 256 different kinds of memory? In James, S. Nairne (Ed.). *The foundations of remembering: Essays in honor of Henry L. Roediger III*, page 39. New York: Psychology Press.

Vogler, G. P. (1985). Multivariate path analysis of familial resemblance. *Genetic Epidemiology*, *2*, 35–53.

von Oertzen, T., Brandmaier, A. M., & Tsang, S. (2015). Structural equation modeling with onyx. *Structural Equation Modeling: A Multidisciplinary Journal*, *22*(1), 148–161.

Wright, S. (1921). Correlation and causation. *Journal of Agricultural Research*, *20*, 557–585.

PROOF