A Test for Comparing the Location of Quadratic Growth Curves

Wanchunzi Yu * Mark Reiser[†]

Abstract

Quadratic growth curves of 2^{nd} degree polynomial are widely used in longitudinal studies. For a 2^{nd} degree polynomial, the vertex gives the location of the curve in the XY plane. We present an approximate confidence region for the vertex using two methods, a gradient method and the delta method. Under some models, an indirect test on the location of the vertex can be based on the intercept and slope parameters, but in other models, a direct test on the vertices is required. We present a quadratic-form statistic for a test of the null hypothesis that there is no shift in the location of the vertex in a mixed linear model. The statistic has an approximate chi-squared distribution. We also present results for a simulation study conducted to assess the influence of sample size and nature of the random effects. Simulation results show that the test statistic performs well in terms of Type I error rate and power. We also present interpretations of shift in the location of the vertex.

Key Words: Vertex, mixed model, quadratic growth curve, confidence region

1. Introduction

The relation between two variables x and y cannot be adequately described by a simple linear regression model in most longitudinal studies. Adding a square of the fixed effect variable x to the model gives a quadratic model, which can often describes the true unknown model very well. When the predictor variable is time, the model becomes a quadratic growth curve model. The coefficient parameters of fixed effect are necessary to determine the regression curve, but they are actually not the matter of interest. The vertex of the quadratic growth curve should be more interesting because it gives the maximum and minimum of such a curve. In practice, by all means reasonable, it is important to derive the confidence region of the parabola's vertex as well as the confidence interval of x and y coordinate. Both the x and y coordinate are given by a non-linear combination of the model coefficient parameters, not simply only one of them. However common statistical computer packages usually display confidence intervals for the model coefficient parameters, but not for any of their functions. Obviously it is reasonable to study it.

The main purpose of this project is to give methods for confidence interval and region of the vertex of a quadratic growth curve mixed model and to perform simulations using different models, parameters and sample sizes to show the validity of these methods and compare them. The methods we focus on are delta method, gradient method and mean response method for confidence interval and approximate chi-square method for confidence region. For the power analysis, different non-vertex points are tested. Different types of covariance structures are also compared in the project.

In Section 2, we make a review of some models and methods used in this project. In Section 3, we give the different methods used in simulation study. Simulation results are analyzed in Section 4. We present the conclusion and discussion in Section 5.

^{*}First author's affiliation, Physical Sciences, A-Wing, P.O. Box 871804, Tempe, AZ 85287-1804

[†]Second author's affiliation, Physical Sciences, A-Wing, P.O. Box 871804, Tempe, AZ 85287-1804

2. Review of Literature

2.1 Delta Method

In statistics, the delta method is a method for deriving an approximate probability distribution for a function of an asymptotically normal statistical estimator from knowledge of limiting variance of that estimator. More broadly, the delta method is known as a generalization of the Central Limit Theorem using Taylor series approximations for mean and variance. Using a Taylor series expansion, if a function g(Y) has derivatives of order r, that is, $g^r(Y) = \frac{d^r}{dy^r}g(Y)$ exists, then for any constant a, the Taylor polynomial of order r about a is,

$$T_r(Y) = \sum_{i=0}^r \frac{g^{(i)}(a)}{i!} (Y-a)^i.$$

Taylor's major theorem is that the remainder from the approximation, $g(Y) - T_r(Y)$ always tends to zero faster than the highest-order explicit term. Thus we can drop the higher-order terms to give the approximation,

$$g(Y) \approx g(a) + g'(a)(Y-a)$$
.

Let $a = \mu$, the mean of Y, a Taylor series expansion of g(Y) about μ gives the approximation,

$$g(Y) = g(\mu) + g'(\mu)(Y - \mu)$$
.

Taking the variance of both sides yields,

$$Var(g(Y)) \approx (g'(\mu))^2 Var(Y)$$
.

For univariate delta method, the function $g(\mathbf{Y})$ is a real-valued continuous function of \mathbf{Y} , for \mathbf{Y} an element of N-dimensional Euclidean space. Let Y_N be a sequence of random variables that satisfies $\sqrt{N}(Y_N - \mu) \rightarrow N(0, \sigma^2)$ in distribution. For a given function gand a specific value of μ , suppose that $g'(\mu)$ exists and is not 0. Then

$$\sqrt{N}(g(Y_N) - g(\mu)) \to N(0, \sigma^2(g'(\mu))^2)$$
 in distribution.

For multivariate delta method, define the random vector $\mathbf{Y} = (Y_1, ..., Y_p)$ with mean $\boldsymbol{\mu} = (\mu_1, ..., \mu_p)$ and covariances $Cov(Y_j, Y_{j'}) = \sigma_{jj'}$. We shall observe N *i.i.d* random samples of the population of \mathbf{Y} and denote these samples as $\mathbf{Y}^{(1)}, ..., \mathbf{Y}^{(N)}$. Furthermore, we call the sample means for each element of the vector $\hat{Y}_j = \sum_{k=1}^N Y_j^{(k)}, \ j = 1, ..., p$ and $\hat{\mathbf{Y}}$ as the vector of sample means. Finally, we consider the multivariate function $g : \mathbb{R} \to \mathbb{R}$ with $g(\mathbf{Y}) = g(Y_1, ..., Y_p)$ and use Taylor expansion to write

$$g(\hat{Y}_1, ..., \hat{Y}_p) \approx g(\mu_1, ..., \mu_p) + \sum_{j=1}^p g'_j(\mu_j)(\hat{Y}_j - \mu_j).$$

In vector notation, this is

$$g(\hat{Y}) \approx g(\boldsymbol{\mu}) + \nabla' g(\boldsymbol{\mu}) (\hat{Y} - \boldsymbol{\mu}),$$

with the abuse of notation that $\nabla' g(\mu) = (\nabla' g(\mathbf{Y}))|_{\mathbf{Y}=\mu}$. The multivariate delta method in vector form is, let $\mathbf{Y}^{(1)}, ..., \mathbf{Y}^{(N)}$ be a random sample with $\mathbf{E}(\mathbf{Y}^{(k)}) = \mu$ and covariance matrix $\mathbf{E}(\mathbf{Y}^{(k)} - \mu)(\mathbf{Y}^{(k)} - \mu)' = \Sigma$. For a given function g with continuous first partial derivatives and a specific value of μ for which $\tau^2 = \nabla' g(\mu) \Sigma \nabla g(\mu) > 0$,

$$\sqrt{N}(g(\hat{\boldsymbol{Y}}) - g(\boldsymbol{\mu})) \to N(\boldsymbol{0}, \tau^2) \text{ in distribution.}$$
(1)

2.2 The Confidence Set for X-Coordinate With a Given Gradient

The univariate classical fixed effects quadratic model is given by

$$y_i = \beta_0 + \beta_1 x_i + \beta_2 x_i^2 + \epsilon_i$$

where $x_i, i = 1, ...N$, denote fixed x-values, y_i denotes the response variable, N is the number of observations and ϵ_i the errors, which are assumed to be independent and normally distributed random variables with an expected value 0 and a common unknown variance $\sigma^2 > 0$. The function $p : x_i \to E(y_i) = \beta_0 + \beta_1 x_i + \beta_2 x_i^2$ is a parabola in x_i . The x-coordinate where this parabola has given gradient m results in

$$x_{gigrad} = \frac{m - \beta_1}{2\beta_2}$$
 Provided that $\beta_2 \neq 0$.

A point estimate of it is given by $\hat{x}_{gigrad} = (m - b_1)/(2b_2)$, where b_1 and b_2 are the least squares estimates. This point estimation is not unbiased. It is that x-coordinate where the empirical regression parabola has the given gradient.

An exact $(1 - \alpha)$ -confidence set for x_{gigrad} is obtained as a solution of function below, where $t_{n-3,1-\alpha/2}^2$ denotes the squared *t*-quantile with n - 3 degrees of freedom, (Martin Bachmaier, A confidence set for that *x*-coordinate where a quadratic regression model has a given gradient, Stat Papers, 50:649-660, 2009.):

$$x_0 \in C(x_{qiqrad})$$

$$\Rightarrow \frac{(b_1 - m + 2x_0b_2)^2}{\hat{Var}(b_1) + 4x_0\hat{Cov}(b_1, b_2) + 4x_0^2\hat{Var}(b_2)} \leqslant t_{n-3,1-\alpha/2}^2$$
(2)
$$\Rightarrow (b_1 - m + 2x_0b_2)^2 \leqslant [\hat{Var}(b_1) + 4x_0\hat{Cov}(b_1, b_2) + 4x_0^2\hat{Var}(b_2)] \cdot t_{n-3,1-\alpha/2}^2$$
$$\Rightarrow A \cdot x_0^2 + B \cdot x_0 + C \leqslant 0 .$$

$$Where, A = b_2^2 - \hat{Var}(b_2) \cdot t_{n-3,1-\alpha/2}^2$$
$$B = (b_1 - m)b_2 - \hat{Cov}(b_1, b_2) \cdot t_{n-3,1-\alpha/2}^2$$
$$C = \frac{1}{4}((b_1 - m)^2 - \hat{Var}(b_1) \cdot t_{n-3,1-\alpha/2}^2) .$$

The medium equivalence sign requires that the denominator in (2) is positive. This is fulfilled if the mean square error is positive. Since the mean square error equals to zero only occurs with probability zero, we can choose an optional confidence interval for this case without violating the coverage probability of the confidence interval.

To solve the inequality, if $A \neq 0$, then $A \cdot x_0^2 + B \cdot x_0 + C$ is a parabola. It has two nulls if the discriminant $D = B^2 - 4AC$ is positive. With regard to the numerical stability concerning small values of 4AC, we compute either zero in two different ways:

$$x_{01} = \frac{-2C}{B - \sqrt{B^2 - 4AC}} \qquad \text{when } B < 0$$
$$= \frac{-B - \sqrt{B^2 - 4AC}}{2A} \qquad \text{when } B \ge 0$$
$$x_{02} = \frac{-B + \sqrt{B^2 - 4AC}}{2A} \qquad \text{when } B \le 0$$
$$= \frac{-2C}{B + \sqrt{B^2 - 4AC}} \qquad \text{when } B \le 0$$

Thus when A > 0 and D > 0, this leads to a two-sided confidence interval $[x_{01}, x_{02}]$. When A < 0 and D > 0, the confidence interval goes to $(-\infty, x_{02}] \bigcup [x_{01}, +\infty)$.

2.3 Interval Estimation for Mean Response

A common objective in regression analysis is to estimate the mean for one or more probability distributions of Y. Let X_h denote the level of X for which we wish to estimate the mean response. X_h may be a value which occurred in the sample, or it may be some other value of the predictor variable within the scope of the model. The mean response when $X = X_h$ is denoted by $E{Y_h}$.

The sampling distribution of \hat{Y}_h refers to the different values of \hat{Y}_h that would be obtained if repeated samples were selected, each holding the levels of the predictor variable X constant, and calculating \hat{Y}_h for each sample. For normal error fixed effects model, the sampling distribution of \hat{Y}_h is normal, with mean $E\{\hat{Y}_h\} = E\{Y_h\}$ and variance $\sigma^2\{\hat{Y}_h\} = \sigma^2[\frac{1}{n} + \frac{(X_h - \bar{X})^2}{\Sigma(X_i - \bar{X})^2}]$. When mean square error (MSE) is substituted for σ^2 , we obtain $s^2\{\hat{Y}_h\}$, the estimated variance of \hat{Y}_h ,

$$s^{2}\{\hat{Y}_{h}\} = MSE[\frac{1}{n} + \frac{(X_{h} - \bar{X})^{2}}{\Sigma(X_{i} - \bar{X})^{2}}]$$

The estimated standard deviation of \hat{Y}_h is then $s\{\hat{Y}_h\}$, the positive square root of $s^2\{\hat{Y}_h\}$. Thus,

$$\frac{\hat{y}_h - E\{y_h\}}{s\{\hat{y}_h\}} \qquad is \ distributed \ as \ t(n-p) \ distribution, \tag{3}$$

where p is the number of regression coefficients. A confidence interval for $E\{Y_h\}$ is constructed in the standard fashion, making use of the t distribution. The $(1 - \alpha)$ confidence limits are,

$$\hat{Y}_h \pm t(1 - \alpha/2; n - p)s\{\hat{Y}_h\}.$$

If there exists vertex $V' = (V_x, V_y)$ of the model, when the value of x-coordinate V_x is known, we could estimate the value of y-coordinate \hat{V}_y by substituting V_x in the regression model and the standard deviation $s\{\hat{V}_y\} = MSE[\frac{1}{n} + \frac{(V_x - \bar{X})^2}{\Sigma(X_i - \bar{X})^2}]$. Using formula(3), then the $(1 - \alpha)$ confidence limits of \hat{V}_y are,

$$\hat{V}_y \pm t(1 - \alpha/2; n - p)s\{\hat{V}_y\}$$
.

3. Methods for Growth Curve Mixed Model

In this report, we consider two growth curve models. One is second-order mixed model with only random intercept, the other is second-order mixed model with random intercept and random slope. Since the predictor variable is time, the two models are both quadratic growth curve. They are defined as follows,

Second-order Mixed model with only random intercept,

$$y_{ij} = \beta_0 + \beta_1 x_{ij} + \beta_2 x_{ij}^2 + \alpha_{0i} + \epsilon_{ij} \qquad i = 1, ..., N \quad j = 1, ..., n$$
(4)

where,

 y_{ij} denotes the response variable for the i^{th} individual at the j^{th} occasion, with $E(y_{ij}) = \beta_0 + \beta_1 x_{ij} + \beta_2 x_{ij}^2$,

n is the number of time points, N is the number of individuals,

 β_0, β_1 and β_2 are regression coefficients of fixed effect,

 α_{0i} is random effect, $\alpha_{0i} \sim N(0, \sigma_{\alpha_0}^2)$,

 ϵ_{ij} are random error terms, $\epsilon_{ij} \sim N(0, \sigma_e^2)$,

 α_{0i} and ϵ_{ij} are independent, $Cov(\alpha_{0i}, \epsilon_{ij}) = 0$ for all *i*.

Second-order Mixed model with random intercept and random slope,

$$y_{ij} = \beta_0 + \beta_1 x_{ij} + \beta_2 x_{ij}^2 + \alpha_{0i} + \alpha_{1i} x_{ij} + \epsilon_{ij} \qquad i = 1, ..., N \quad j = 1, ..., n$$
(5)

where,

 y_{ij} denotes the response variable for the i^{th} individual at the j^{th} occasion, with $E(y_{ij}) = \beta_0 + \beta_1 x_{ij} + \beta_2 x_{ij}^2$,

n is the number of time points, N is the number of individuals,

 β_0, β_1 and β_2 are regression coefficients of fixed effect,

 α_{0i} and α_{1i} are independent random effects, with $\alpha_{0i} \sim N(0, \sigma_{\alpha_0}^2)$, $\alpha_{1i} \sim N(0, \sigma_{\alpha_1}^2)$ and $Cov(\alpha_{0i}, \alpha_{1i}) = 0$ for all *i*,

$$\epsilon_{ij}$$
 are random error terms, $\epsilon_{ij} \sim N(0, \sigma_e^2)$,

 α_{0i}, α_{1i} and ϵ_{ij} are independent, $Cov(\alpha_{0i}, \epsilon_{ij}) = 0$ and $Cov(\alpha_{1i}, \epsilon_{ij}) = 0$ for all *i*.

Let $\mathbf{b}' = (b_0, b_1, b_2)$ be the Generalized Least Square estimator of $\boldsymbol{\beta}' = (\beta_0, \beta_1, \beta_2)$. Under some situations, the distribution of $\hat{\boldsymbol{\beta}}$ is exact. More generally, \boldsymbol{b} is approximately normally distributed with mean $\boldsymbol{\beta}$ and covariance $Cov(\mathbf{b})$, i.e., $\mathbf{b} \stackrel{a}{\sim} (\boldsymbol{\beta}, Cov(\mathbf{b}))$. Where,

$$Cov(\mathbf{b}) = \begin{pmatrix} \sigma_{b_0}^2 & \sigma_{b_0b_1} & \sigma_{b_0b_2} \\ \sigma_{b_0b_1} & \sigma_{b_1}^2 & \sigma_{b_1b_2} \\ \sigma_{b_0b_2} & \sigma_{b_1b_2} & \sigma_{b_2}^2 \end{pmatrix} .$$

Then the estimated covariance of Cov(b) could be expressed as

$$\hat{Cov}(\boldsymbol{b}) = \begin{pmatrix} \hat{\sigma}_{b_0}^2 & \hat{\sigma}_{b_0b_1} & \hat{\sigma}_{b_0b_2} \\ \hat{\sigma}_{b_0b_1} & \hat{\sigma}_{b_1}^2 & \hat{\sigma}_{b_1b_2} \\ \hat{\sigma}_{b_0b_2} & \hat{\sigma}_{b_1b_2} & \hat{\sigma}_{b_2}^2 \end{pmatrix} .$$

Since, both mixed models are quadratic growth curve, there exists a vertex if the quadratic coefficient $\beta_2 \neq 0$. Let $V' = (V_x, V_y)$ be the vertex of mixed model (4) or model (5). Then,

$$V_x(\beta_1, \beta_2) = -\frac{1}{2}\beta_1\beta_2^{-1} ,$$

$$V_y(\beta_0, \beta_1, \beta_2) = \beta_0 - \frac{1}{4}\beta_1^2\beta_2^{-1}$$

Let $\hat{V}' = (\hat{V}_x, \hat{V}_y)$ be the estimated vertex. Then,

$$\hat{V}_x(b_1, b_2) = -rac{1}{2}b_1b_2^{-1} \; ,$$

 $\hat{V}_y(b_0, b_1, b_2) = b_0 - rac{1}{4}b_1^2b_2^{-1} \; .$

For the vertex $V' = (V_x, V_y)$, the first derivative with respect to β is,

$$\frac{\partial \mathbf{V}}{\partial \boldsymbol{\beta}} = \begin{pmatrix} 0 & -\frac{1}{2}\beta_2^{-1} & \frac{1}{2}\beta_1\beta_2^{-2} \\ 1 & -\frac{1}{2}\beta_1\beta_2^{-1} & \frac{1}{4}\beta_1^2\beta_2^{-2} \end{pmatrix} \,.$$

Similarly, for the estimated vertex $\hat{V}' = (\hat{V}_x, \hat{V}_y)$, the first derivative evaluated at $\beta = b$ is,

$$\frac{\partial \mathbf{V}}{\partial \boldsymbol{\beta}}\Big|_{\boldsymbol{\beta}=\boldsymbol{b}} = \left(\begin{array}{ccc} 0 & -\frac{1}{2}b_2^{-1} & \frac{1}{2}b_1b_2^{-2} \\ 1 & -\frac{1}{2}b_1b_2^{-1} & \frac{1}{4}b_1^2b_2^{-2} \end{array} \right) \; .$$

3.1 Confidence Region

3.1.1 Delta Method for Confidence Interval of coordinate X and Y

When sample size goes large, \hat{V} is normally distributed with mean V and asymptotic covariance $Cov(\hat{V})$. Where

$$Cov(\hat{\boldsymbol{V}}) = \frac{\partial \boldsymbol{V}}{\partial \boldsymbol{\beta}} Cov(\boldsymbol{b}) \frac{\partial \boldsymbol{V}}{\partial \boldsymbol{\beta}'} \\ = \begin{pmatrix} \sigma_{\hat{V}_x}^2 & \sigma_{\hat{V}_x} \hat{V}_y \\ \sigma_{\hat{V}_x \hat{V}_y} & \sigma_{\hat{V}_y}^2 \end{pmatrix}$$

Let $\hat{Cov}(\hat{V})$ be the estimated asymptotic covariance of estimated vertex, then

$$\hat{Cov}(\hat{V}) = \frac{\partial V}{\partial \beta} \hat{Cov}(b) \frac{\partial V}{\partial \beta'} \Big|_{\beta=b} \\
= \begin{pmatrix} \hat{\sigma}_{\hat{V}_x}^2 & \hat{\sigma}_{\hat{V}_x} \hat{V}_y \\ \hat{\sigma}_{\hat{V}_x} \hat{V}_y & \hat{\sigma}_{\hat{V}_y}^2 \end{pmatrix},$$
(6)

where,

$$\hat{\sigma}_{\hat{V}_x}^2 = (0, -\frac{1}{2}b_2^{-1}, \frac{1}{2}b_1b_2^{-2}) \cdot \hat{Cov}(\boldsymbol{b}) \cdot (0, -\frac{1}{2}b_2^{-1}, \frac{1}{2}b_1b_2^{-2})',$$

$$\hat{\sigma}_{\hat{V}_y}^2 = (1, -\frac{1}{2}b_1b_2^{-1}, \frac{1}{4}b_1^2b_2^{-2}) \cdot \hat{Cov}(\boldsymbol{b}) \cdot (1, -\frac{1}{2}b_1b_2^{-1}, \frac{1}{4}b_1^2b_2^{-2})'.$$

Let $\boldsymbol{\theta} = (\boldsymbol{\beta}', \boldsymbol{\alpha}')'$ as the parameter vector and $\boldsymbol{y} = \boldsymbol{f}(\boldsymbol{\theta}), \, \boldsymbol{y} \in \mathbb{R}^n$. Let $\boldsymbol{\theta}^*$ be the true parameter vector, then under $H_0 : \boldsymbol{\theta}^* \in \Theta_0 \subset R^s$,

- 1. θ^* is an interior point of Θ_0 and there is an *s*-dimensional neighborhood of θ^* completely contained in Θ_0 , thus the variance is greater than zero.
- 2. The mapping $f : \Theta_0 \mapsto y$ in totally differentiate at θ^* so that partial derivative of f_i with respect to θ_j exist at θ^* and $f(\theta)$ has a linear approximation at θ^* given by first-order Taylor series expansion.
- 3. The Jacobian matrix $\frac{\partial f(\theta^*)}{\partial \theta}$ is of full rank.
- 4. The mapping $f: \Theta_0 \mapsto y$ is continuous at every point $\theta \in \Theta_0$.

Thus the multivariate delta method(1) could be used by satisfying all the conditions. When sample size goes large, \hat{V} , the estimate of V, is approximately multivariate normally distributed with mean V and covariance $Cov(\hat{V})$, i.e., $\hat{V} \stackrel{a}{\sim} MVN(V, Cov(\hat{V}))$. By using the estimated covariance $\hat{Cov}(\hat{V})$ for $Cov(\hat{V})$, \hat{V}_x is approximately normal distributed with mean V_x and variance $\sigma^2_{\hat{V}_x}$, i.e. $\hat{V}_x \stackrel{a}{\sim} N(V_x, \sigma^2_{\hat{V}_x})$. Similarly, \hat{V}_y is approximately normal distributed with mean V_y and variance $\sigma^2_{\hat{V}_y}$, i.e. $\hat{V}_y \stackrel{a}{\sim} N(V_y, \sigma^2_{\hat{V}_y})$.

Thus, the approximate $(1 - \alpha)\%$ confidence interval of \hat{V}_x is $(\hat{V}_x - Z_{1-\alpha/2}\hat{\sigma}_{\hat{V}_x}, \hat{V}_x + Z_{1-\alpha/2}\hat{\sigma}_{\hat{V}_x})$. Similarly, the approximate $(1 - \alpha)\%$ confidence interval of \hat{V}_y is $(\hat{V}_y - Z_{1-\alpha/2}\hat{\sigma}_{\hat{V}_y}, \hat{V}_y + Z_{1-\alpha/2}\hat{\sigma}_{\hat{V}_y})$.

3.1.2 Gradient Method for Confidence Interval of Coordinate X

When given a gradient, formula (2) could be used to compute a confidence interval. For testing the vertex of a quadratic mixed model, the gradient equals to zero, that is m = 0. When θ is unknown, the distribution of $\hat{\theta}$ is approximately normal in large sample. Then the distribution of \hat{V} is approximately normal and the normal distribution should be used instead of t distribution in the confidence intervals for V_x and V_y . Thus an adjusted formula (2) for confidence interval of x-coordinate of the vertex is,

$$x_{0} \in C(V_{x})$$

$$\Leftrightarrow \frac{(b_{1} + 2x_{0}b_{2})^{2}}{\hat{\sigma}_{b_{1}}^{2} + 4x_{0}\hat{\sigma}_{b_{1}b_{2}} + 4x_{0}^{2}\hat{\sigma}_{b_{2}}^{2}} \leqslant Z_{1-\alpha/2}^{2}$$

$$\Leftrightarrow (b_{1} + 2x_{0}b_{2})^{2} \leqslant [\hat{\sigma}_{b_{1}}^{2} + 4x_{0}\hat{\sigma}_{b_{1}b_{2}} + 4x_{0}^{2}\hat{\sigma}_{b_{2}}^{2}] \cdot Z_{1-\alpha/2}^{2}$$

$$\Leftrightarrow A \cdot x_{0}^{2} + B \cdot x_{0} + C \leqslant 0 .$$

$$Where, A = b_{2}^{2} - \hat{\sigma}_{b_{2}}^{2} \cdot Z_{1-\alpha/2}^{2}$$

$$B = b_{1}b_{2} - \hat{\sigma}_{b_{1}b_{2}} \cdot Z_{1-\alpha/2}^{2}$$

$$C = \frac{1}{4}(b_{1}^{2} - \hat{\sigma}_{b_{1}}^{2} \cdot Z_{1-\alpha/2}^{2}) .$$

$$(7)$$

To solve the inequality, if $A \neq 0$, then $A \cdot x_0^2 + B \cdot x_0 + C$ in formula(7) is a parabola. It has two nulls if the discriminant $D = B^2 - 4AC$ is positive. With regard to the numerical stability concerning small values of 4AC, we compute either zero in two different ways:

$$x_{01} = \frac{-2C}{B - \sqrt{B^2 - 4AC}} \qquad when B < 0$$

$$= \frac{-B - \sqrt{B^2 - 4AC}}{2A} \qquad when B \ge 0$$

$$x_{02} = \frac{-B + \sqrt{B^2 - 4AC}}{2A} \qquad when B \le 0$$

$$= \frac{-2C}{B + \sqrt{B^2 - 4AC}} \qquad when B > 0$$
(9)

Thus when A > 0 and D > 0, this leads to a two-sided confidence interval $[x_{01}, x_{02}]$. When A < 0 and D > 0, the confidence interval goes to $(-\infty, x_{02}] \bigcup [x_{01}, +\infty)$. In this report, we only consider the first situation. Then the confidence interval of coordinate X for vertex \hat{V}_x is $[x_{01}, x_{02}]$.

3.1.3 Mean Response Method for Confidence Interval of Coordinate Y

If the x-coordinate of the vertex \hat{V}_x is substituted into the regression model,

$$\hat{y_{ij}} = b_0 + b_1 x_{ij} + b_2 x_{ij}^2$$

the y-coordinate of vertex \hat{V}_y could be calculated as,

$$\hat{V}_y = b_0 + b_1 \cdot \hat{V}_x + b_2 \cdot \hat{V}_x^2$$

Here \hat{V}_y could be treated as a mean response of y when $x = \hat{V}_x$ and $E\{V_y\} = V_y$, $s\{\hat{V}_y\} = \hat{\sigma}_{\hat{V}_y}$. Since θ is unknown, the normal distribution should be used instead of the t distribution when sample size goes large as usual. Thus for y-coordinate of vertex \hat{V}_y ,

$$\frac{\hat{V}_y - V_y}{\hat{\sigma}_{\hat{V}_y}^2} \sim N(0, 1) \; ,$$

where $\hat{\sigma}_{\hat{V}_y}^2 = (1, \hat{V}_x, \hat{V}_x^2) \cdot \hat{Cov}(b) \cdot (1, \hat{V}_x, \hat{V}_x^2)'.$ Thus the $(1 - \alpha)\%$ confidence interval of V_y is $(\hat{V}_y - Z_{1-\alpha/2}\hat{\sigma}_{\hat{V}_y}, \hat{V}_y + Z_{1-\alpha/2}\hat{\sigma}_{\hat{V}_y}).$

Since $\hat{V_x} = -\frac{1}{2}b_1b_2^{-1}$ and $\hat{V_x}^2 = \frac{1}{4}b_1^2b_2^{-2}$, then

$$\hat{\sigma}_{\hat{V}_y}^2 = (1, -\frac{1}{2}b_1b_2^{-1}, \frac{1}{4}b_1^2b_2^{-2}) \cdot \hat{Cov}(\boldsymbol{b}) \cdot (1, -\frac{1}{2}b_1b_2^{-1}, \frac{1}{4}b_1^2b_2^{-2})'.$$

It is exactly same as the estimated variance of V_y from the delta method. Thus, the result of these two methods should be exactly same.

3.1.4 Confidence Region for Vertex

The large sample chi-square distribution for a quadratic form could be used to compute a confidence region. The chi-square distribution with k degrees of freedom is the distribution of a sum of the squares of k independent standard normal random variables. We have already proved that the estimated vertex follows an approximate multivariate normal distribution,

$$\hat{\boldsymbol{V}} \stackrel{a}{\sim} MVN(\boldsymbol{V}, Cov(\hat{\boldsymbol{V}}))$$
.

For the bivariate standard normal distribution in vector form, the sum of the squares of two independent standard normal variables is chi-square distribution with 2 degrees of freedom:

$$\begin{pmatrix} \hat{V}_x - V_x \\ \hat{V}_y - V_y \end{pmatrix}' Cov(\hat{\boldsymbol{V}})^{-1} \begin{pmatrix} \hat{V}_x - V_x \\ \hat{V}_y - V_y \end{pmatrix} \stackrel{a}{\sim} \chi^2_{(2)} .$$

Because $\hat{Cov}(\hat{V})$ is consistent for $Cov(\hat{V})$, substituting $\hat{Cov}(\hat{V})$ for $Cov(\hat{V})$, an approximate chi-square distribution with 2 degrees of freedom could be used,

$$\begin{pmatrix} \hat{V}_x - V_x \\ \hat{V}_y - V_y \end{pmatrix}' \hat{Cov}(\hat{\boldsymbol{V}})^{-1} \begin{pmatrix} \hat{V}_x - V_x \\ \hat{V}_y - V_y \end{pmatrix} \stackrel{a}{\sim} \chi^2_{(2)} .$$
 (10)

Thus the approximate $(1 - \alpha)\%$ confidence region of the vertex is

$$\begin{pmatrix} \hat{V}_x - V_x \\ \hat{V}_y - V_y \end{pmatrix}' \hat{Cov} (\hat{\boldsymbol{V}})^{-1} \begin{pmatrix} \hat{V}_x - V_x \\ \hat{V}_y - V_y \end{pmatrix} \leqslant \chi^2_{1-\alpha,2} ,$$

we conclude that the confidence region for vertex is an ellipse from this equation.

3.2 Power Analysis

The power of a statistical test is the probability that the test will reject the null hypothesis when the null hypothesis is actually false. In this study, it is important to reject the null hypothesis point if it is not the vertex; this is power analysis. For example,

$$H_0: \mathbf{V} = \mathbf{V}_0 \quad v.s. \quad H_a: \mathbf{V} = \mathbf{V}_a$$

where V_0 is not the vertex, V_a is the vertex.

The large sample chi-square distribution for a quadratic form could be used to compute a p-value similar to computing the confidence region. Let $V'_0 = (V_{0x}, V_{0y})$ be the non-vertex tested point. Under null hypothesis, a chi-square distribution with 2 degrees of freedom should be followed,

$$\begin{pmatrix} \hat{V}_x - V_{0x} \\ \hat{V}_y - V_{0y} \end{pmatrix}' Cov(\hat{V})^{-1} \begin{pmatrix} \hat{V}_x - V_{0x} \\ \hat{V}_y - V_{0y} \end{pmatrix} \sim \chi^2_{(2)} .$$

Similarly, because $\hat{Cov}(\hat{V})$ is consistent for $Cov(\hat{V})$, when sample size is large enough, substituting $\hat{Cov}(\hat{V})$ for $Cov(\hat{V})$, an approximate chi-square distribution with 2 degrees of freedom could be used

$$\begin{pmatrix} \hat{V}_x - V_{0x} \\ \hat{V}_y - V_{0y} \end{pmatrix}' \hat{Cov} (\hat{V})^{-1} \begin{pmatrix} \hat{V}_x - V_{0x} \\ \hat{V}_y - V_{0y} \end{pmatrix} \stackrel{a}{\sim} \chi^2_{(2)} .$$
 (11)

Thus reject the null hypothesis if

$$\begin{pmatrix} \hat{V}_x - V_{0x} \\ \hat{V}_y - V_{0y} \end{pmatrix}' \hat{Cov} (\hat{V})^{-1} \begin{pmatrix} \hat{V}_x - V_{0x} \\ \hat{V}_y - V_{0y} \end{pmatrix} > \chi^2_{1-\alpha,2} .$$

4. Analysis of Simulation Results

Simulation studies are performed for the mixed model with only random intercept and for the model with both random intercept and random slope. For each model, we construct the confidence intervals for the x and y coordinate of the vertex using two different methods and compare them. Confidence region and power analysis are also studied. Although the methods derived in this project are from large sample size, we also want to check whether the methods work for small sample size. Thus sample size 100, 50 and 20 are chosen for the simulation studies, Type I error rate is chosen to be 0.01, 0.05 and 0.5. We choose six time points for the growth curve mixed model, that is, every individual is measured six times, without missing data.

4.1 Simulation Results for Mixed Model with only Random Intercept

For mixed model with only random intercept (4), we generate 1000 data sets with the same coefficient parameters β_0 , β_1 and β_2 equal to 2, 8 and -1, and $\sigma_{\alpha_0}^2$ equals to 1 for sample size 100, 50 and 20. Thus the true model is,

$$y_{ij} = 2 + 8x_{ij} - x_{ij}^2 + \alpha_{0i} + \epsilon_{ij}, \qquad i = 1, 2, ..., N \quad j = 1, 2, ..., 6.$$

Then,

$$E\{y_{ij}\} = 2 + 8x_{ij} - x_{ij}^2, \qquad i = 1, 2, ..., N \quad j = 1, 2, ..., 6.$$

The true vertex of this quadratic growth curve is V' = (4, 18).

The covariance structure should be decided before simulation. We examine the covariance structures UN, CS and AR(1), and compare SAS default criteria AIC, BIC and AICC. All the three criteria show minimum values when the covariance structure is compound symmetry. Also the mixed model we generated is a quadratic function, the within-subject factor is randomly allocated to subjects, it should be the compound symmetry. Thus we choose the compound symmetry as covariance structure for all the 1000 data sets in this simulation.

Type I	Sample	Coverage	lower	upper	Coverage	lower	upper
Error	Size	I	bound	bound	II	bound	bound
0.01	100	0.985	0.9751	0.9949	0.984	0.97378	0.99422
0.01	50	0.984	0.97378	0.99422	0.987	0.97778	0.99622
0.01	20	0.984	0.97378	0.99422	0.983	0.97247	0.99353
0.05	100	0.940	0.92528	0.95472	0.937	0.92194	0.95206
*0.05	50	0.932	0.9164	0.9476	0.935	0.91972	0.95028
0.05	20	0.944	0.92975	0.95825	0.945	0.93087	0.95913
0.1	100	0.887	0.87053	0.90347	0.890	0.87372	0.90628
0.1	50	0.888	0.87159	0.90441	0.886	0.86947	0.90253
0.1	20	0.888	0.87159	0.90441	0.890	0.87372	0.90628

 Table 1: Confidence Intervals for X-Coordinate

 Table 2: Confidence Intervals for Y-Coordinate of Vertex

Type I	Sample	Coverage	lower	upper	Coverage	lower	upper
Error	Size	I	bound	bound	II	bound	bound
0.01	100	0.990	0.98190	0.99810	0.990	0.98190	0.99810
0.01	50	0.981	0.96988	0.99212	0.981	0.96988	0.99212
0.01	20	0.984	0.97378	0.99422	0.984	0.97378	0.99422
0.05	100	0.942	0.92751	0.95649	0.942	0.92751	0.95649
0.05	50	0.945	0.93087	0.95913	0.945	0.93087	0.95913
0.05	20	0.941	0.92640	0.95560	0.941	0.92640	0.95560
0.1	100	0.896	0.88012	0.91188	0.896	0.88012	0.91188
0.1	50	0.899	0.88333	0.91467	0.899	0.88333	0.91467
*0.1	20	0.88	0.86310	0.89690	0.88	0.86310	0.89690

4.1.1 Simulation Results for Confidence Interval

The results of simulation for confidence intervals of x-coordinate are shown in Table.1. In this table, symbol I represents delta method and symbol II represents gradient method. The results include the coverage as well as lower bound and upper bound for the coverage. To obtain the coverage p in this report, when a confidence interval contains the true value it is coded as 1, otherwise 0; then the count is obtained and divided by the total number of data sets 1000. The count follows a binomial distribution with mean 1000p and variance 1000p(1-p). Thus the standard deviation of coverage $p = \frac{count}{1000}$ is $\sqrt{\frac{p(1-p)}{1000}}$ and the bounds on the true coverage are obtained from $p \pm Z_{1-\alpha/2}\sqrt{\frac{p(1-p)}{1000}}$. From the columns of coverage, only one of the 18 conditions had coverage outside the bounds; it is sample size 50 and Type I error 0.05 delta method. Thus we conclude that both methods are applicable for the confidence interval for different sample sizes tested.

The results of simulation for confidence intervals of y-coordinate are shown in Table.2. In this table, symbol I represents delta method and symbol II represents mean response method. The results include the coverage as well as lower bound and upper bound for the coverage. From the columns of coverage, two of the 18 conditions had coverage outside the bounds; they are sample size 20 and Type I error 0.1 both methods. It seems that respect to the y-coordinate, when sample size is small, the two methods are not quite good. However, the other four conditions, sample size 20 and Type I error 0.01 and 0.05 all give good results. We can conclude that both methods are usable for the confidence intervals. But small sample size must be given more attention.

In section 3, we proved that although the two methods come from different approaches, the results of them should be exactly same. Table.2 showed that not only the coverage, but also the lower and upper bound are exactly same.



Figure 1: Confidence Region of Vertex

			0	
Type I	Sample	Coverage	lower	upper
Érror	Size	I	bound	bound
0.01	100	0.988	0.97913	0.99687
0.01	50	0.985	0.97510	0.99490
0.01	20	0.98	0.96860	0.99140
*0.05	100	0.933	0.91750	0.94850
0.05	50	0.936	0.92083	0.95117
0.05	20	0.941	0.92640	0.95560
0.1	100	0.889	0.87266	0.90534
0.1	50	0.884	0.86734	0.90066
0.1	20	0.886	0.86947	0.90253

Table 3: Confidence Region of Vertex

4.1.2 Simulation Results for Confidence Region

In Section 3.1.4, we have shown that the confidence region should be an ellipse. Figure.1 shows the model used in the simulation, i.e. $E\{y\} = 2 + 8x + x^2$. For the plot, the value of chi-square, 599, is chosen as it is 100 times of 5.99 (the value of chi-square distribution with two degrees of freedom when Type I error equals 0.05) to make the ellipse clear. If the value is too small, the ellipse in the plot will reduce to a dot. The results of the simulation for the confidence region of the vertex are shown in Table.3. The results include the coverage as well as lower bound and upper bound for the coverage. From the column of coverage, only one of the 9 conditions had coverage outside the bounds; it is sample size 100 and Type I error 0.05. Although we use the approximate chi-square distribution with two degrees of freedom, we conclude that the method is practicable for confidence region for different sample sizes tested.

4.1.3 Simulation Results for Power Analysis

The results of simulation for power are shown in Table.4. The null hypothesis is chosen based on the difference of 0.05 and 0.1 between the point under the null hypothesis and true vertex. We test all the pairwise combinations of these points. The results include the power as well as lower bound and upper bound for the interval around the empirical power. From the table, when we keep V_{0x} as the true value, the change of V_{0y} does not affect the power much. However, when we keep V_{0y} as the true value, the change of V_{0x} affects the power much more. The result means that the x-coordinate is more sensitive than y-coordinate. The width of y-coordinate confidence interval are commonly larger than xcoordinate confidence interval, which means that the variation of y-coordinate is larger than x-coordinate. It is because the number of time points we choose for x is only 6, but the range of y-coordinate is much larger than x. Finally, we simulate when the null hypothesis is the true vertex, and the empirical power is nearly equal to the size of the test.

V_{0x}	V_{0y}	Power	Lower bound	Upper bound			
3.95	18.05	0.671	0.64188	0.70012			
3.95	17.95	0.657	0.62758	0.68642			
3.95	18.1	0.712	0.68393	0.74007			
3.95	17.9	0.694	0.66544	0.72256			
3.9	18.05	0.999	0.99704	1.00096			
3.9	17.95	0.999	0.99704	1.00096			
3.9	18.1	0.999	0.99704	1.00096			
3.9	17.9	0.999	0.99704	1.00096			
4.05	18.05	0.644	0.61432	0.67368			
4.05	17.95	0.653	0.62350	0.68250			
4.05	18.1	0.673	0.64392	0.70208			
4.05	17.9	0.7	0.6716	0.7284			
4.1	18.05	0.994	0.98921	0.99879			
4.1	17.95	0.995	0.99063	0.99937			
4.1	18.1	0.994	0.98921	0.99879			
4.1	17.9	0.995	0.99063	0.99937			
4	18	0.067	0.051503	0.082497			

Table 4: Power (N=100, $\alpha = 0.05$)

4.2 Simulation Results for Mixed Model with Random Intercept and Slope

For mixed model with random intercept and slope (5), we also generate 1000 data sets with the same coefficient parameters β_0 , β_1 and β_2 equal to 2, 8 and -1, and $\sigma_{\alpha_0}^2$, $\sigma_{\alpha_1}^2$ and $\sigma_{\alpha_0,\alpha_1}$ equal to 1, 0.5 and 0 for sample size 100, 50 and 20. Thus the true model is,

$$y_{ij} = 2 + 8x_{ij} - x_{ij}^2 + \alpha_{0i} + \alpha_{1i}x_{ij} + \epsilon_{ij}, \qquad i = 1, 2, ..., N \quad j = 1, 2, ..., 6.$$

Then,

$$E\{y_{ij}\} = 2 + 8x_{ij} - x_{ij}^2, \qquad i = 1, 2, ..., N \quad j = 1, 2, ..., 6.$$

The true vertex of this quadratic growth curve is V' = (4, 18).

To choose the covariance structure, we proceed as before. After comparing the AIC, BIC and AICC, we found that when covariance structure is unstructured, all the three criteria are minimum.

4.2.1 Simulation Results for Confidence Interval

The results of simulation for confidence intervals of X-coordinate with covariance structure UN are shown in Table.5. In this table, symbol I represents delta method and symbol II represents gradient method. The results include the coverage as well as lower bound and upper bound for the coverage. In Table.5, four of the 18 conditions had coverage outside the bounds; they are sample size 100 and Type I error 0.1 both methods and sample size 20 and Type I error 0.1 both methods. Thus we conclude that both the methods are available for the confidence interval for different sample sizes tested.

The results of simulation for confidence intervals of y-coordinate with covariance structure UN are shown in Table.6. In this table, symbol I represents delta method and symbol II represents mean response method. The results include the coverage as well as lower bound and upper bound for the coverage. In Table.6, four of the 18 conditions had coverage outside the bounds; they are sample size 100 and Type I error 0.1 both methods and sample size 20 and Type I error 0.05 both methods.

Type I	Sample	Coverage	lower	upper	Coverage	lower	upper
Érror	Size	I	bound	bound	II	bound	bound
0.01	100	0.984	0.97378	0.99422	0.985	0.97510	0.99490
0.01	50	0.983	0.97247	0.99353	0.982	0.97117	0.99283
0.01	20	0.986	0.97643	0.99557	0.985	0.97510	0.99490
0.05	100	0.945	0.93087	0.95913	0.944	0.92975	0.95825
0.05	50	0.94	0.92528	0.95472	0.939	0.92417	0.95383
0.05	20	0.938	0.92305	0.95295	0.937	0.92194	0.95206
*0.1	100	0.879	0.86204	0.89596	0.876	0.85886	0.89314
0.1	50	0.89	0.87372	0.90628	0.889	0.87266	0.90534
*0.1	20	0.882	0.86522	0.89878	0.882	0.86522	0.89878

 Table 5: Confidence Intervals for X-Coordinate with UN

Table 6: Confidence Intervals for Y-Coordinate with UN

Type I	Sample	Coverage	lower	upper	Coverage	lower	upper
Error	Size	I	bound	bound	II	bound	bound
0.01	100	0.989	0.98051	0.99749	0.989	0.98051	0.99749
0.01	50	0.991	0.98331	0.99869	0.991	0.98331	0.99869
0.01	20	0.984	0.97378	0.99422	0.984	0.97378	0.99422
0.05	100	0.941	0.92640	0.95560	0.941	0.92640	0.95560
0.05	50	0.938	0.92305	0.95295	0.938	0.92305	0.95295
*0.05	20	0.933	0.91750	0.94850	0.933	0.91750	0.94850
*0.1	100	0.88	0.86310	0.89690	0.88	0.86310	0.89690
0.1	50	0.892	0.87585	0.90815	0.892	0.87585	0.90815
0.1	20	0.889	0.87266	0.90534	0.889	0.87266	0.90534

4.2.2 Simulation Results for Confidence Region

The simulation results for confidence region of the vertex with covariance structure UN are shown in Table.7. The results include the coverage as well as lower bound and upper bound for the coverage. In Table.7, from the column of coverage, only one of the 9 conditions had coverage outside the bounds; it is sample size 50 and type I error 0.05. Thus we can conclude that the approximate chi-square distribution used for confidence region is applicable for different sample sizes tested.

4.2.3 Simulation Results for Power Analysis

We investigate the simulation of power with only covariance structure UN based on the conclusion of confidence interval and confidence region. The results of simulation are shown in Table.8. The points to be tested are chosen based on the difference of 0.05 and

Type I	Sample	Coverage	lower	upper				
Error	Size	I	bound	bound				
0.01	100	0.99	0.98190	0.99810				
0.01	50	0.986	0.97643	0.99557				
0.01	20	0.984	0.97378	0.99422				
0.5	100	0.936	0.92083	0.95117				
0.5	50	0.936	0.92083	0.95117				
0.5	20	0.94	0.92528	0.95472				
0.1	100	0.886	0.86947	0.90253				
*0.1	50	0.875	0.85780	0.89220				
0.1	20	0.885	0.86840	0.90160				

Table 7: Confidence Region of Vertex with UN

	Iuble	. 10.001	(11 100, a 0.0	, 01()
V_{0x}	V_{0y}	Power	Lower bound	Upper bound
3.95	18.05	0.594	0.56356	0.62444
3.95	17.95	0.397	0.36667	0.42733
3.95	18.1	0.689	0.66031	0.71769
3.95	17.9	0.326	0.29695	0.35505
3.9	18.05	0.994	0.98921	0.99879
3.9	18.1	0.997	0.99361	1.00039
3.9	17.9	0.964	0.95245	0.97555
3.9	17.95	0.977	0.96771	0.98629
4.05	18.05	0.442	0.41122	0.47278
4.05	18.1	0.348	0.31848	0.37752
4.05	17.95	0.604	0.57369	0.63431
4.05	17.9	0.69	0.66133	0.71867
4.1	18.05	0.952	0.93875	0.96525
4.1	18.1	0.935	0.91972	0.95028
4.1	17.95	0.984	0.97622	0.99178
4.1	17.9	0.993	0.98783	0.99817
4	18	0.064	0.048830	0.079170

Table 8: Power (N=100, $\alpha = 0.05$, UN)

0.1 between the point under the null hypothesis and true vertex. We test all the pairwise combinations of these points. The results include the power as well as lower bound and upper bound for the interval around the empirical power.

From the table, when we keep V_{0x} equal to the true value, the change of V_{0y} does not affect the power much. However, when we keep V_{0y} equal to the true value, the change of V_{0x} extremely affects the results. It means that the x-coordinate is more sensitive than the y-coordinate. The reason is similar as the mixed model with only random intercept. The width of y-coordinate confidence interval is commonly larger than x-coordinate confidence interval, which means that the variation of y-coordinate is larger than x-coordinate. It is because the number of time points we choose for x-coordinate is only 6, but the range of ycoordinate is much larger than x-coordinate. Finally, we simulate when the null hypothesis is the true vertex, the result shows the empirical power is nearly equal to the size of the test.

5. Conclusion and Discussion

Several methods for confidence interval and confidence region for the vertex of the mixed quadratic growth curve model were discussed in this report. Initially, delta method and gradient method were performed for the confidence interval of x-coordinate of the vertex, while delta method and mean response method for the y-coordinate. The approximate chi-square distribution with two degrees of freedom were derived in the confidence region analysis and power analysis. Furthermore, in the simulation study, two models, mixed model with only random intercept and mixed model with random intercept and random slope, were considered. For each model, three different sample sizes were chosen in order to examine the influence of size for all the methods. Three different Type I error rates were chosen as well for the purpose of making the methods more convincible. The different types of covariance structure were compared for these two different mixed model. Results show that compound symmetry is the best for mixed model with only random intercept while unstructured is the best for mixed model with random intercept and slope, which conforms to the properties of different models. Depending on all the simulation results, a conclusion could be drawn that all methods described in this study for confidence region of the vertex of quadratic growth curves of 2^{nd} degree polynomial are applicable for different sample sizes, different Type I error rates and different models. For the power analysis,

some non-vertex points were tested to show the efficiency of the methods as well as the relationship between confidence region and power.

An interesting topic for further research can be dealing with two different samples, such as treatment and control groups. A test for switch in the location of the vertices might be performed. One the other hand, for only one sample, number of measurement time points should be considered as the influence of confidence region for the vertex. Covariates also could be added in the regression model; the change of vertex with covariates may be examined.

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