PIECEWISE LINEAR MIXED EFFECTS MODELING

ROSENKRANZ LAB MEETING

ESTELLE HIGGINS

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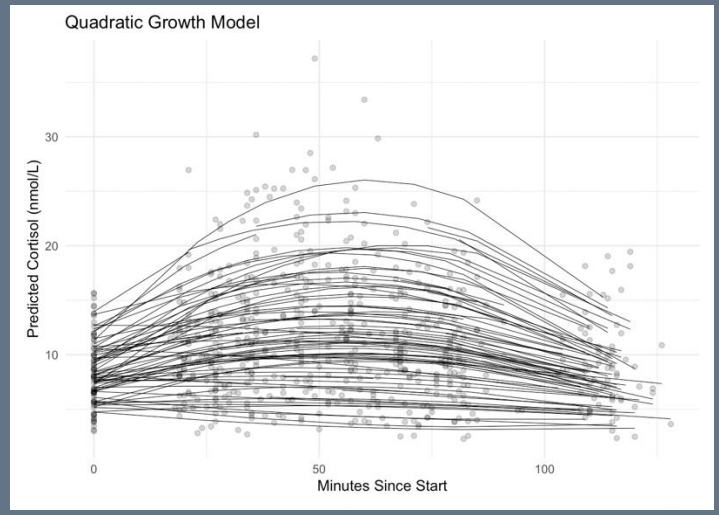
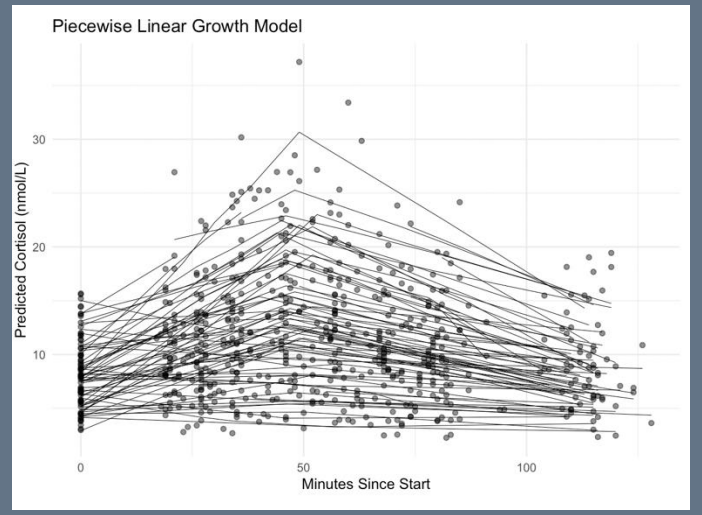
WHEN DO YOU NEED PIECEWISE?

- Data with different linear trends over different regions
  - x-y relationship is a continuous function with 2+ linear segments
- Clear break points (“knots”)
- Theoretically-motivated questions
  - Longitudinal data

WHY PIECEWISE AND NOT POLYNOMIAL?

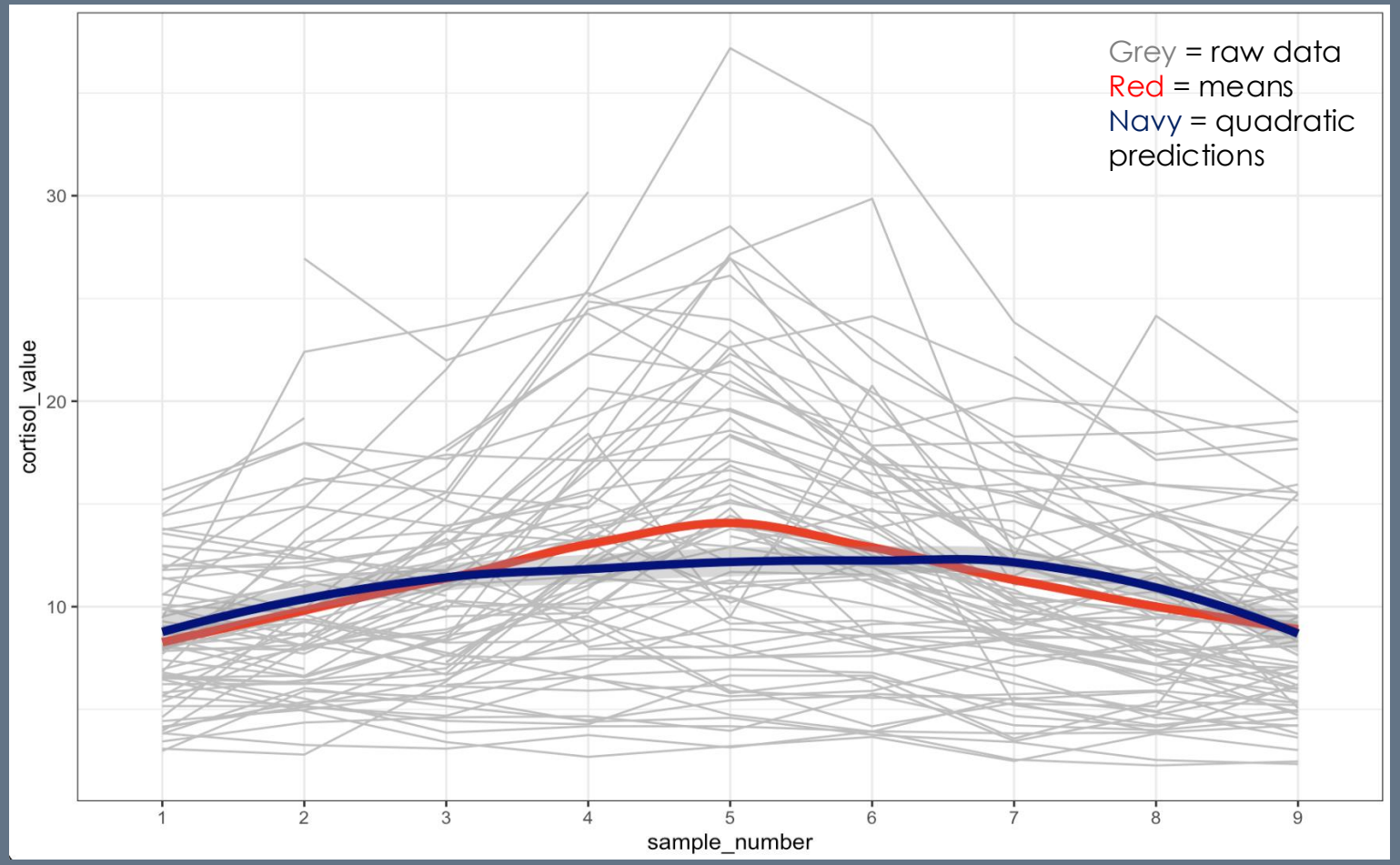
- Interpretation
  - *slope estimates at various stages; distinct "growth phases"*
  - *identify locations of meaningful change in slope*
  - Polynomial assumes **smooth trajectory**
- Piecewise allows you to examine how different "pieces" relate to other variables
- Avoid multicollinearity
- Piecewise with polynomial pieces





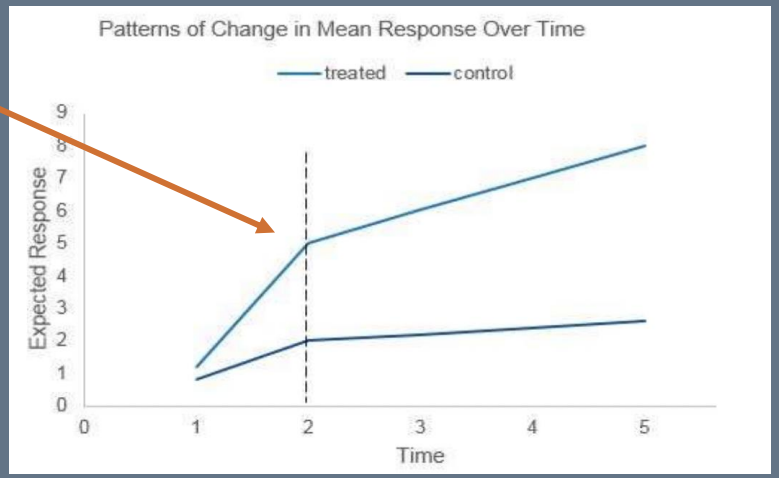
WHY PIECEWISE AND NOT POLYNOMIAL?

- Which fits better?



CHANGE POINTS ("KNOTS")

- x-values where linear function slope changes
- Continuous or discontinuous
- Theory + Data:
  - is change point a known parameter?
  - estimate from data?
- R package SEGMENTED
  - *Determine change points to minimize SSE*



$$y = \beta_{01} + \beta_1 x \qquad for\ x \leq 2$$
$$y = \beta_{02} + \beta_2 x \qquad for\ x \geq 2$$

(image: Huang, 2015)

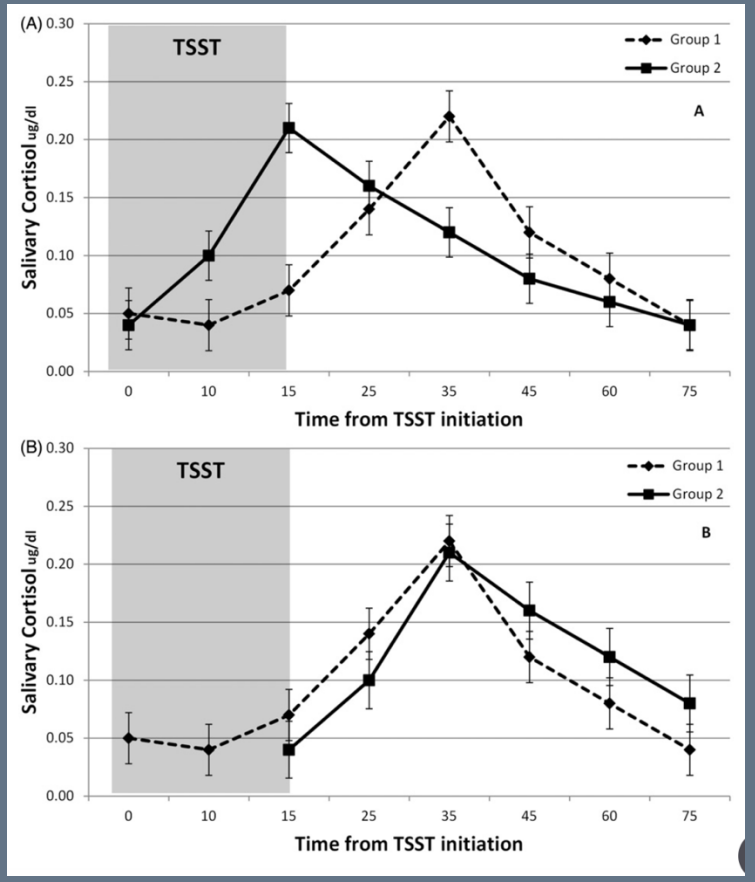
SIDE NOTE:
VARIED CHANGE POINTS

- Is **person-specific timing of change point** of interest?
  - *e.g., onset of cognitive decline*
- Increase model flexibility (fit)
- Change point in random effects structure?
  - Bayesian approach (Brilleman et al., 2017, Epidemiology)
- What if both location *and* number of change points is unknown?

Lopez-Duran et al., 2014, Stress

SIDE NOTE:
VARIED CHANGE POINTS / LANDMARK REGISTRATION

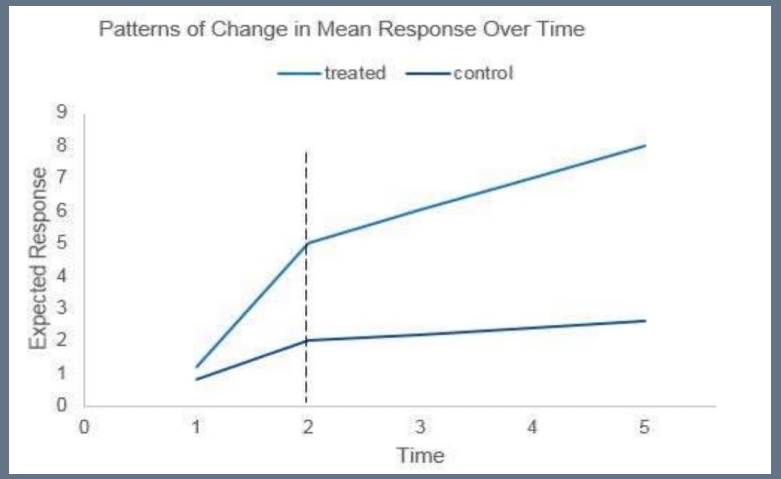
- Control for individual/group difference in time latency of change points
- Example: groups do not differ in reactivity or recovery after adjusting for timing differences



Lopez-Duran et al., 2014, Stress

THE MATH

- Continuous piecewise regression
  - 2+ equations
  - Equal at change points



$$y = \beta_{01} + \beta_1 x \qquad for\ x \leq 0$$
$$y = \beta_{02} + \beta_2 x \qquad for\ x \geq 0$$

$$\beta_{01} + \beta_1 * c = \beta_{02} + \beta_2 * c$$
$$\beta_{01} + \beta_1 * c = \beta_{02} + \beta_2 * c$$
$$\beta_{02} = \beta_{01} + c(\beta_1 - \beta_2)$$

(image: Huang, 2015)

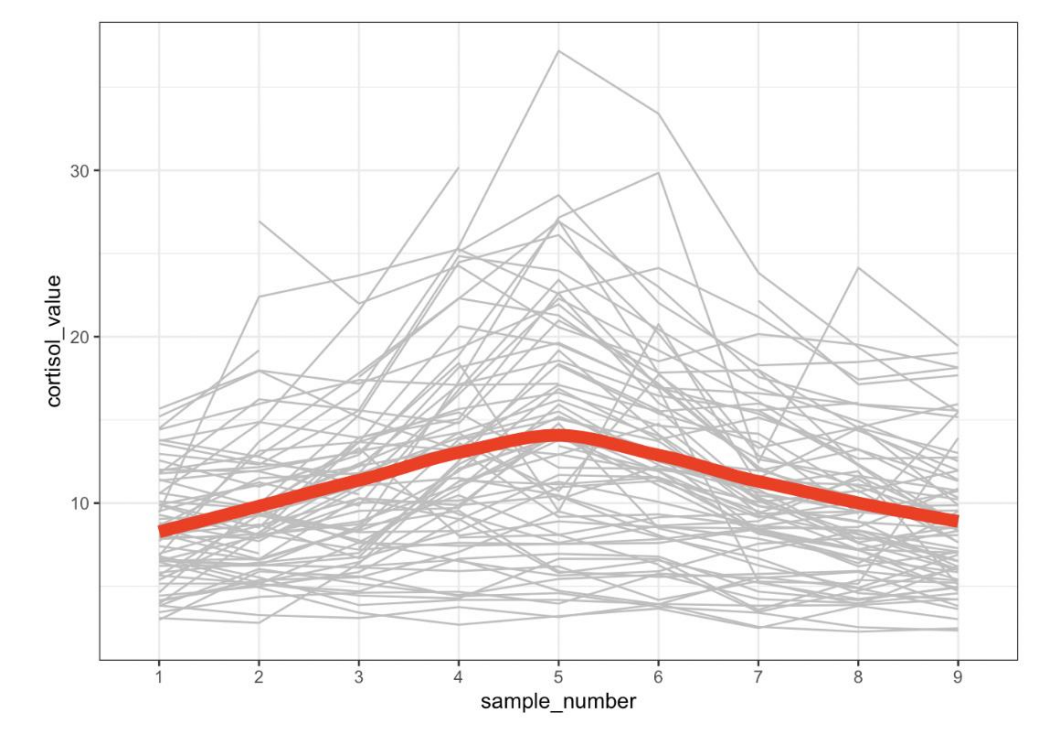
THE MATH

$$y(x) = \begin{cases} \beta_0^1 + \beta_1^1(x - b_1) + e^1 & b_1 \le x \le b_2 \\ \beta_0^2 + \beta_1^2(x - b_2) + e^2 & b_2 < x \le b_3 \\ \vdots & \vdots \\ \beta_0^{n-1} + \beta_1^{n-1}(x - b_{n-1}) + e^{n-1} & b_{n-1} < x \le b_n \end{cases}$$

- b_1 = *x* location of first break
- b_2 = *x* location of second break point
- b_n = *x* location of n^{th} break point

PIECEWISE LMEMS

EXAMPLE



EXAMPLE: DATA

Dummy Code Contrast

- $x_{i2} = 0$ for $x_{i1} < k$
- $x_{i2} = 1$ for $x_{i1} > k$

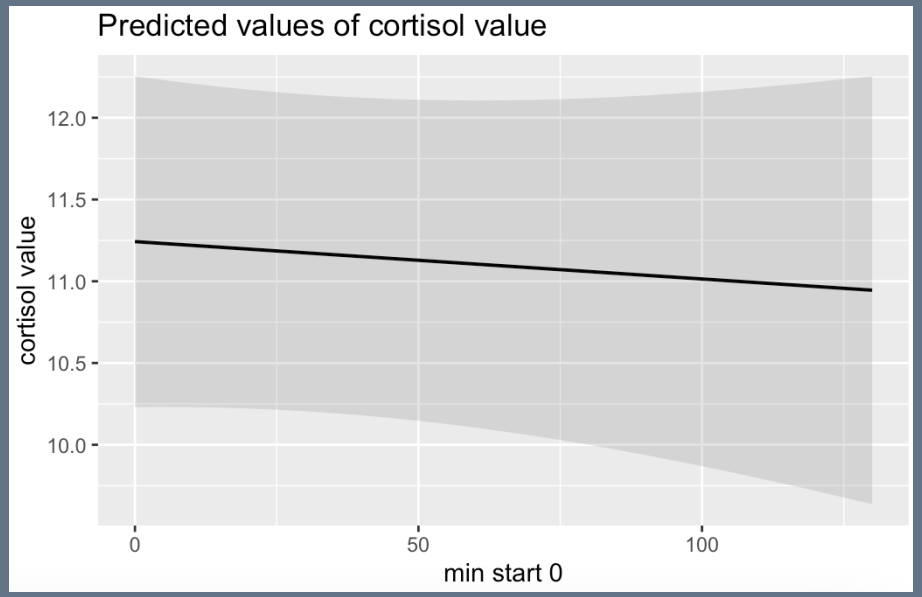
$$y_i = \beta_0 + \beta_1 x_{i1} + \beta_2 (x_{i1} - \boldsymbol{k}) x_{i2} + \epsilon_i$$

subid	sample_num	time_to_peak_mean	reac	recov	cortisol_value
1001	1	-48	-48	0	15.2
1001	2	-26	-26	0	17.95
1001	3	-18	-18	0	15.16
1001	4	-11	-11	0	13.19
1001	5	0	0	0	9.17
1001	6	11	0	11	9.32
1001	7	22	0	22	8.62
1001	8	33	0	33	9.44
1001	9	65	0	65	10.73
1002	1	-48	-48	0	6.62
1002	2	-26	-26	0	6.28
1002	3	-18	-18	0	6.13
1002	4	-11	-11	0	5.91
1002	5	0	0	0	6.19
1002	6	11	0	11	4.18
1002	7	22	0	22	5.31
1002	8	33	0	33	3.9
1002	9	65	0	65	6.23
1003	1	-48	-48	0	10.57
1003	2	-26	-26	0	14.79
1003	3	-18	-18	0	21.55
1003	4	-11	-11	0	30.18
1003	5	0	0	0	NA
1003	6	11	0	11	25.32
1003	7	22	0	22	NA
1003	8	33	0	33	14.65
1003	9	65	0	65	9.88
1004	1	-48	-48	0	9.04

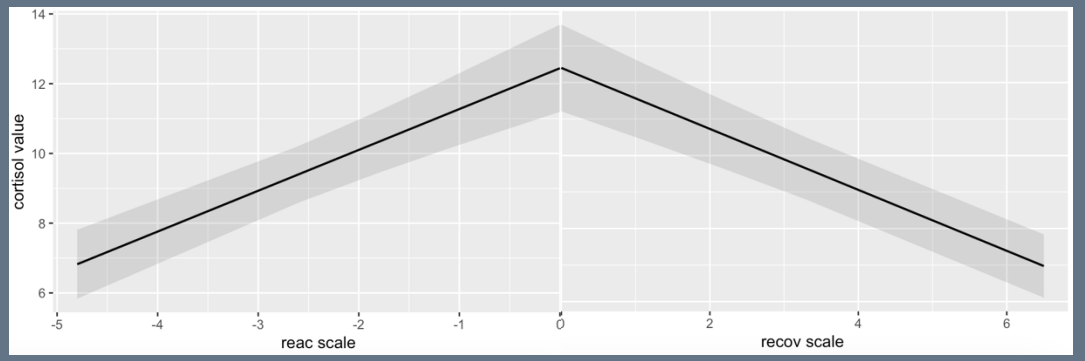
EXAMPLE: MODEL

- Linear growth (not piecewise):

lmer(cortisol ~ time + (1 + time | subid), data)



EXAMPLE: MODEL



- Piecewise linear growth:

lmer(cortisol ~ time1 + time2 + (1 + time1 + time2 | subid), data)

= lmer(cortisol ~ reac + recov + (1 + reac + recov | subid), data)

Level-1: $Cort_{ij} = \beta_{0j} + \beta_{1j} reac_{ij} + \beta_{2j} recov_{ij} + \epsilon_{ij}$

Level-2:

$\beta_{0j} = \gamma_{00} + e_{0j}$ = group avg peak cortisol

$\beta_{1j} = \gamma_{10} + e_{1j}$ = effect of reactivity on cortisol

$\beta_{2j} = \gamma_{20} + e_{2j}$ = effect of recovery on cortisol

$$Cort_{ij} = \gamma_{00} + e_{0j} + (\gamma_{10} + e_{1j}) * reac_{ij} + (\gamma_{20} + e_{2j}) * recov_{ij} + \epsilon_{ij}$$

by-subj random intercept

by-subj random slopes

residual error

Model: lmer(cortisol ~ reac + recov + (1 + reac + recov | subid), data)

EXAMPLE: OUTPUT

- Random Effects:
  - int: betw-subj variance in average peak cortisol
  - reac: betw-subj variance of reactivity slope
  - recov: betw-subj variance of recovery slope
- Fixed Effects:
  - int: average cortisol at peak
  - reac: slope of increase in cort before peak
  - recov: slope of decrease in cort after peak

```
REML criterion at convergence: 3323.8

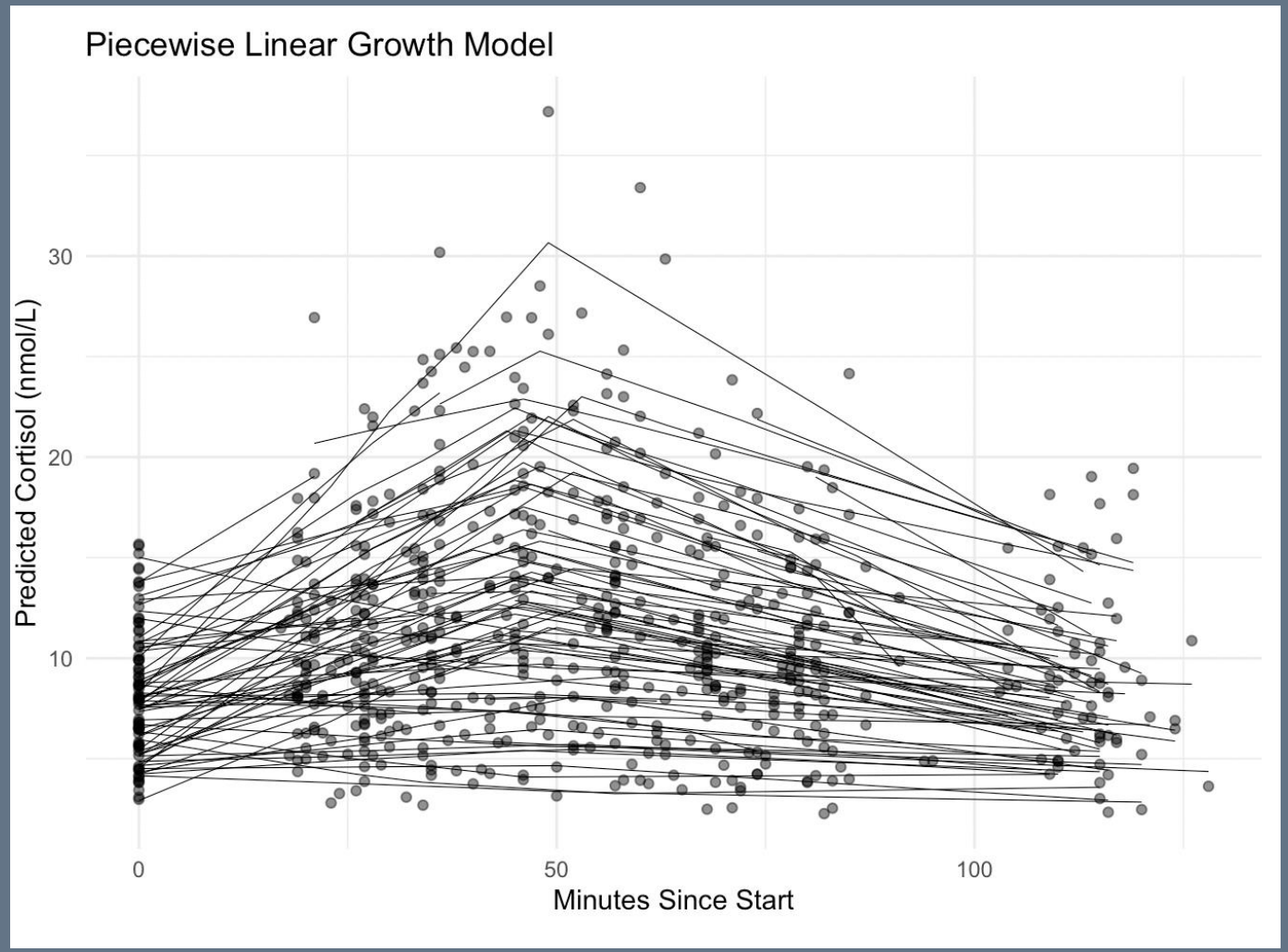
Scaled residuals:
    Min      1Q  Median      3Q     Max
-3.2765 -0.4739 -0.0076  0.4554  3.4436

Random effects:
 Groups   Name        Variance Std.Dev. Corr
 subid    (Intercept) 40.0834  6.3311
          reac_scale   1.6474  1.2835    0.84
          recov_scale  0.4604  0.6786   -0.86 -0.85
 Residual              5.7301  2.3938
Number of obs: 639, groups:  subid, 77

Fixed effects:
            Estimate Std. Error      df t value Pr(>|t|)
(Intercept)  13.6996     0.7409 75.1920  18.489  < 2e-16 ***
reac_scale    1.1708     0.1632 74.6427   7.176 4.43e-10 ***
recov_scale  -0.8349     0.0931 74.8453  -8.968 1.75e-13 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Correlation of Fixed Effects:
            (Intr) rc_scl
reac_scale   0.803
recov_scale -0.783 -0.753
```

EXAMPLE


Piecewise Linear Growth Model
Predicted Cortisol (nmol/L)
30
20
10
0
50
100
Minutes Since Start

MORE COMPLEX MODELS

- How does each piece relate to other variables?
  - *e.g., do those with higher life stress recover more slowly from acute stress?*

MORE COMPLEX MODELS: MATH

Q: does lifetime stress moderate cortisol reactivity and/or recovery from acute stress?

Level-1: $Cort_{ij} = \beta_{0j} + \beta_{1j} reac_{ij} + \beta_{2j} recov_{ij} + \epsilon_{ij}$

Level-2:

$$\beta_{0j} = \gamma_{00} + \gamma_{01} stress_j + e_{0j}$$
$$\beta_{1j} = \gamma_{10} + \gamma_{11} stress_j + e_{1j}$$
$$\beta_{2j} = \gamma_{20} + \gamma_{21} stress_j + e_{2j}$$

γ_{00}: group avg peak cortisol and
γ_{01}: main effect of stress on cortisol (peak)
γ_{10}: main effect of reactivity on cortisol and
γ_{11}: interaction between reac and stress
γ_{20}: main effect of recovery on cortisol and
γ_{21}: interaction between recov and stress

$$Cort_{ij} = \gamma_{00} + \gamma_{01} stress_j + e_{0j} + (\gamma_{10} + \gamma_{11} stress_j + e_{1j}) * reac_{ij} + (\gamma_{20} + \gamma_{21} stress_j + e_{2j}) * recov_{ij} + \epsilon_{ij}$$

by-subj random intercept

by-subj random slopes

residual error

MORE COMPLEX MODELS: R

lmer(cortisol ~ reac*stress + recov*stress + (1 + reac + recov | id))

```
Random effects:
 Groups   Name        Variance Std.Dev. Corr
 subid    (Intercept) 40.6154  6.3730
          reac_scale   1.6111  1.2693    0.84
          recov_scale  0.4541  0.6738   -0.87 -0.90
 Residual              5.8873  2.4264
Number of obs: 546, groups:  subid, 66

Fixed effects:
                     Estimate Std. Error       df t value Pr(>|t|)
(Intercept)         13.810321   0.805874 63.511361  17.137  < 2e-16 ***
reac_scale           1.265459   0.174957 62.199578   7.233 8.35e-10 ***
stress_c            -0.029991   0.027514 63.285098  -1.090   0.2798
recov_scale         -0.865245   0.100524 62.872620  -8.607 3.16e-12 ***
reac_scale:stress_c -0.005826   0.005926 60.779749  -0.983   0.3294
stress_c:recov_scale  0.006075   0.003421 62.226329   1.776   0.0807 .
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Correlation of Fixed Effects:
            (Intr) rc_scl strss_ rcv_sc rc_s:_
reac_scale   0.799
stress_c     0.001  0.001
recov_scale -0.789 -0.789 -0.002
rc_scl:str_  0.001  0.001  0.804 -0.003
strss_c:rc_ -0.002 -0.003 -0.791  0.005 -0.795
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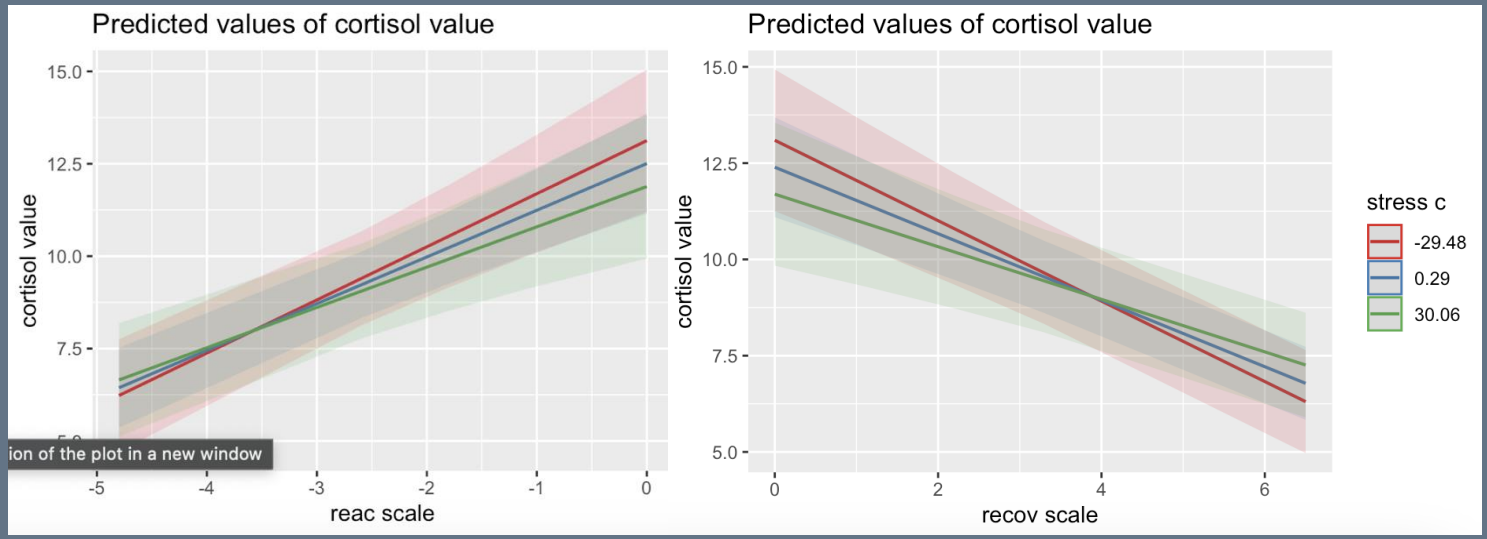
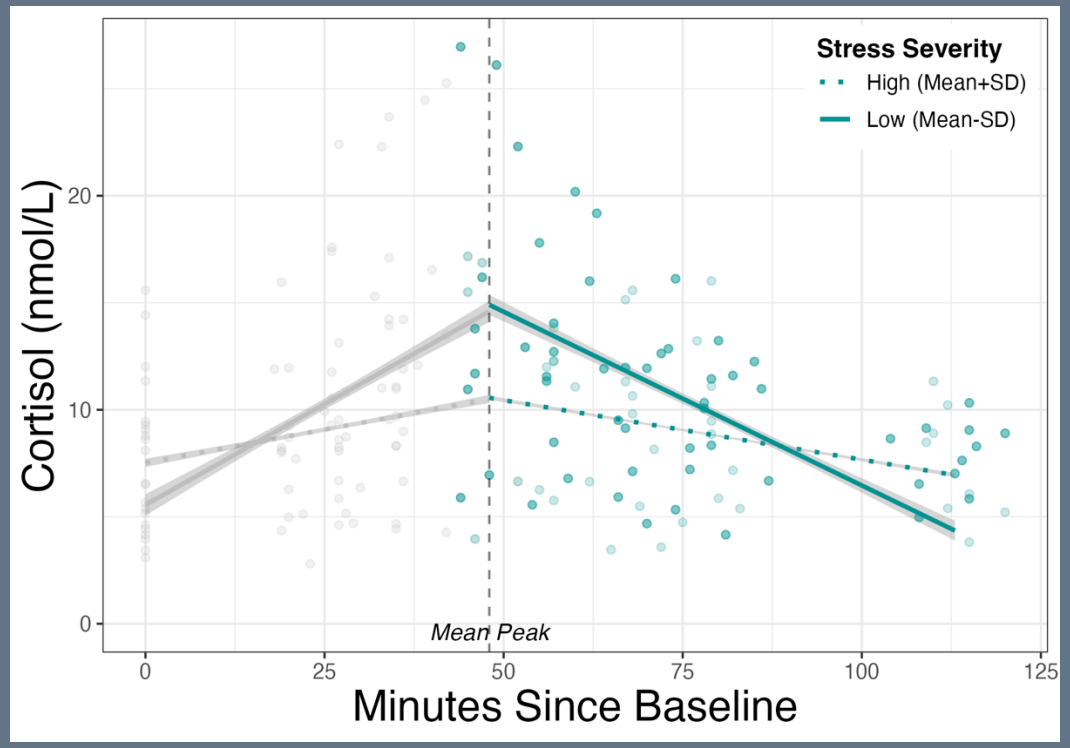
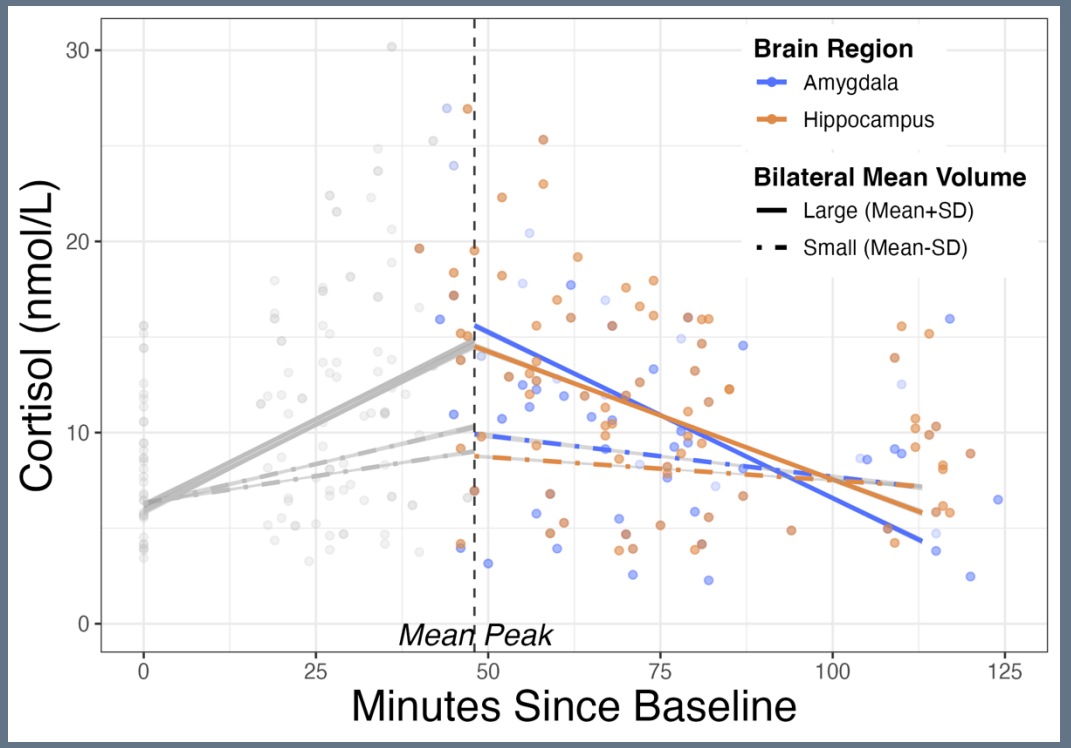


MORE COMPLEX MODELS: VISUALS



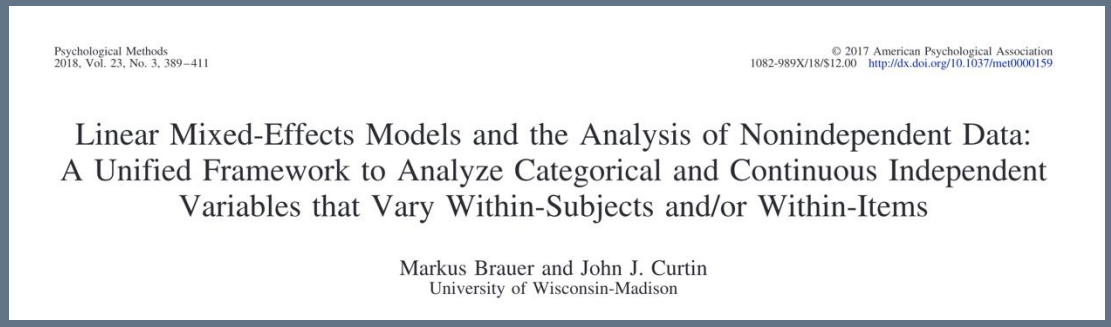


EVEN MORE COMPLEX MODELS: R

```
lmer(cortisol_value ~
        reac*(age + sex + race + icv + stress + amyg + hpc) +
        recov*(age + sex + race + icv + stress + amyg + hpc) +
        (1 + reac + recov | id))
```

Convergence… 😬

- Scale reac/recov by a factor of 10
- Use different optimizers
- *etc.*



Psychological Methods
2018, Vol. 23, No. 3, 389–411

1082-989X/18/$12.00 http://dx.doi.org/10.1037/met0000159

Linear Mixed-Effects Models and the Analysis of Nonindependent Data: A Unified Framework to Analyze Categorical and Continuous Independent Variables that Vary Within-Subjects and/or Within-Items

Markus Brauer and John J. Curtin
University of Wisconsin-Madison

REMAINING QUESTIONS / FUTURE

- Piece trajectories re functional neuroimaging
  - Subject-specific slope estimates
- Significant relationships between pieces
  - e.g., is reactivity steeper than recovery?

RESOURCES

- Daniel Martin tutorial – *R code plus cool plots*
- Huang, 2015 tutorial – *in SAS but helpful mathematical explanations*
- Penn State tutorial
- Info/code on random change points

CORTISOL-SPECIFIC STUDIES (THANKS, CLAIRE!)

- Bendezú, J. J., Loughlin-Presnal, J. E., & Wadsworth, M. E. (2019). Attachment Security Moderates Effects of Uncontrollable Stress on Preadolescent Hypothalamic–Pituitary–Adrenal Axis Responses: Evidence of Regulatory Fit. *Clinical Psychological Science*, *7*(6), 1355–1371. https://doi.org/10.1177/2167702619854747
- Bendezú, J. J., & Wadsworth, M. E. (2017). If the coping fits, use it: Preadolescent recent stress exposure differentially predicts post-TSST salivary cortisol recovery. *Developmental Psychobiology*, *59*(7), 848–862. https://doi.org/10.1002/dev.21542
- Fiksdal, A., Hanlin, L., Kuras, Y., Gianferante, D., Chen, X., Thoma, M. V., & Rohleder, N. (2019). Associations between symptoms of depression and anxiety and cortisol responses to and recovery from acute stress. *Psychoneuroendocrinology*, *102*, 44–52. https://doi.org/10.1016/j.psyneuen.2018.11.035
- Glier, S., Campbell, A., Corr, R., Pelletier-Baldelli, A., Yefimov, M., Guerra, C., Scott, K., Murphy, L., Bizzell, J., & Belger, A. (2022). Coordination of autonomic and endocrine stress responses to the Trier Social Stress Test in adolescence. *Psychophysiology*, *59*(9), e14056. https://doi.org/10.1111/psyp.14056
- Ji, J., Negriff, S., Kim, H., & Susman, E. J. (2016). A study of cortisol reactivity and recovery among young adolescents: Heterogeneity and longitudinal stability and change. *Developmental Psychobiology*, *58*(3), 283–302. https://doi.org/10.1002/dev.21369
- Lopez-Duran, N. L., Mayer, S. E., & Abelson, J. L. (2014). Modeling neuroendocrine stress reactivity in salivary cortisol: Adjusting for peak latency variability. *Stress (Amsterdam, Netherlands)*, *17*(4), 285–295. https://doi.org/10.3109/10253890.2014.915517