① **For each time point *s* in trial photometry traces:**
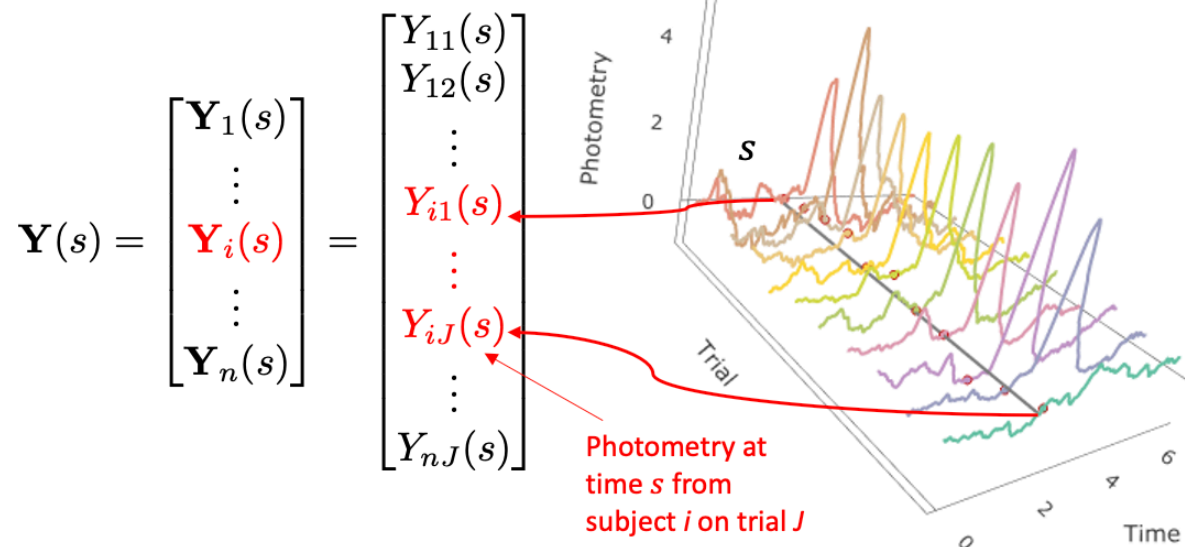- Collect photometry signal values at time point *s* of each trial from all animals and sessions and concatenate into a single common vector: $\mathbf{Y}(s)$

$$\mathbf{Y}(s) = \begin{bmatrix} \mathbf{Y}_1(s) \\ \vdots \\ \mathbf{Y}_i(s) \\ \vdots \\ \mathbf{Y}_n(s) \end{bmatrix} = \begin{bmatrix} Y_{11}(s) \\ Y_{12}(s) \\ \vdots \\ Y_{i1}(s) \\ \vdots \\ Y_{iJ}(s) \\ \vdots \\ Y_{nJ}(s) \end{bmatrix}$$

Photometry at time *s* from subject *i* on trial *J*

- Regress photometry signal $\mathbf{Y}(s)$ onto covariates **X** (e.g., behavior, cue-type), in a (multivariate) linear mixed model. Covariates take one value *per trial* but are free to affect the photometry signal at each time point, *s*, differently
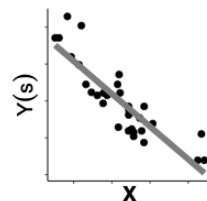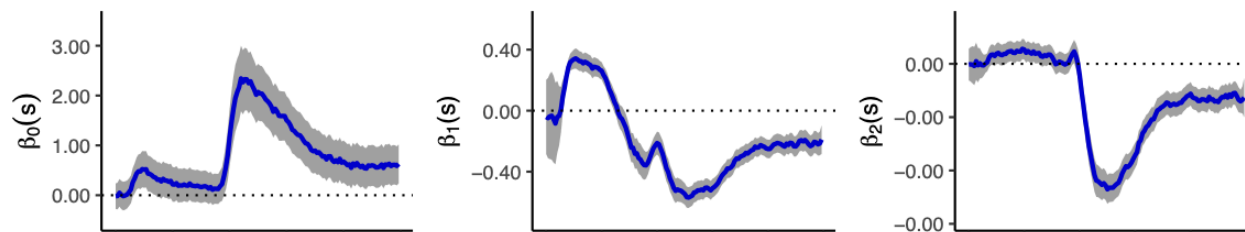
$$\mathbf{Y}_i(s) = \mathbb{X}_i\boldsymbol{\beta}(s) + \mathbb{Z}_i\boldsymbol{\gamma}_i(s) + \boldsymbol{\epsilon}_i(s)$$

- Save regression coefficient estimates associated with each covariate *k* at time point *s*: $\hat{\beta}_k(s)$
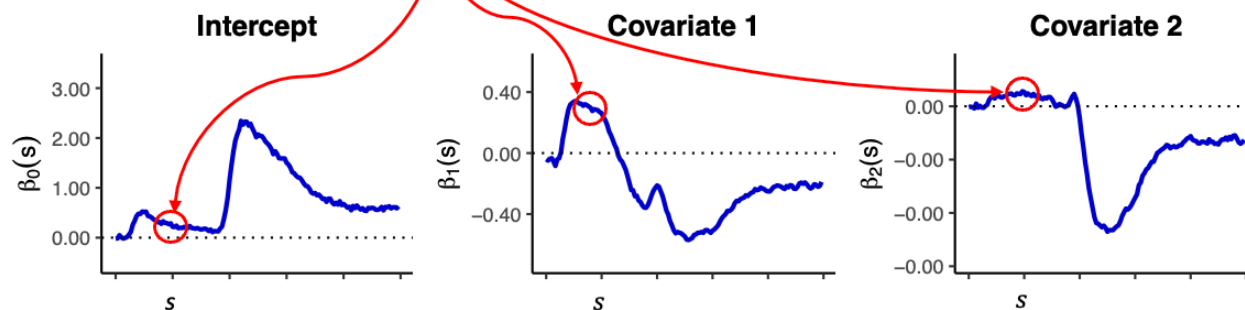
- Calculate *point-wise* 95% confidence intervals (CIs) for coefficients at time point *s*

This yields one vector (length *S*) of estimated $\hat{\boldsymbol{\beta}}_k$ for each covariate *k*

Intercept   **Covariate 1**   **Covariate 2**