1 Data

Name	Symbol	Dimension
Replicates		R
Samples		N
Timepoints		T
Genes		D
Confounders		Q
Expression	$\mathbf{Y}$	$NRT \times D$
Latent Variables of Confounders	$\mathbf{X}$	$NRT \times Q$
Confounders	$\mathbf{C}$	$NRT \times D$

Table 1: Data explanation

2 Assumption on Confounder influence

The confounders are assumed to additively contribute to gene expression:

$$\mathbf{Y} = \mathbf{Y}_{\text{true}} + \mathbf{C} + \sigma^2 \mathbf{I} \ , \tag{1}$$

where in the linear case the confounders are

$$\mathbf{C} = \mathbf{X}\mathbf{W} \tag{2}$$

3 Confounder Simulation

3.1 Linear

$$\mathbf{X} = \text{randn}(NRT, Q) \tag{3}$$
$$\mathbf{W} = \text{randn}(Q, D) \tag{4}$$
$$\mathbf{C} = \mathbf{X}\mathbf{W} \tag{5}$$

4 Confounder Learning

GPLVM: $p(\mathbf{Y}|\mathbf{X}, \mathbf{t}, \mathbf{t}', \boldsymbol{\theta}) = \mathcal{N}(\mathbf{Y}|\mathbf{0}, \mathbf{K}(\mathbf{X}, \mathbf{t}, \mathbf{t}', \boldsymbol{\theta}))$ In the following we will discuss different choices of $\mathbf{K}(X, t, t', \theta)$

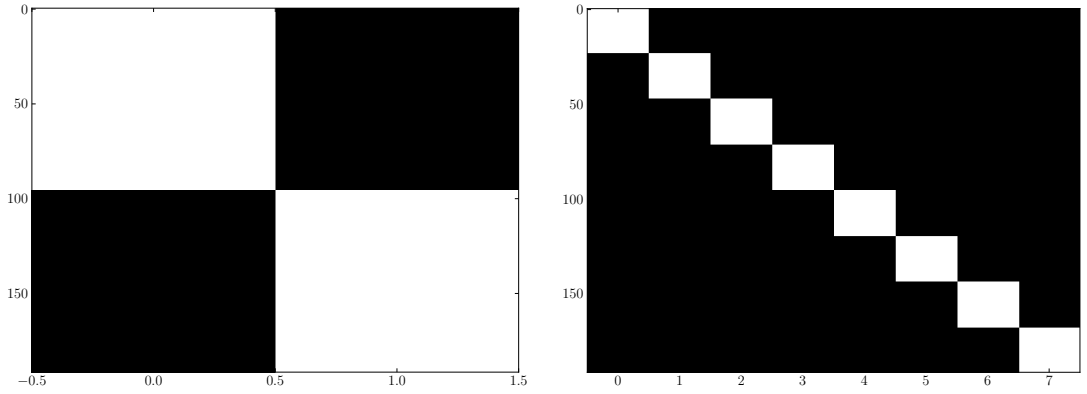
4.1 Different Learning Structures

See Figure 4.1

4.2 Different Learning Models

all Learn confounders excluding all structures, sample structre, replicate structure and sample structure over time

$$p(\mathbf{Y}) = N\big(\mathbf{Y}|\mathbf{0}, \mathbf{X}\mathbf{X}^\top + \mathbf{X}_S\mathbf{X}_S^\top + \mathbf{X}_R\mathbf{X}_R^\top + \mathbf{X}_S\mathbf{X}_S^\top \circ \mathbf{K}(\mathbf{t}, \mathbf{t}')\big) \tag{6}$$



(a) Sample Structure $\mathbf{X}_S$ (b) Replicate Structure $\mathbf{X}_R$

rep Learn confounders excluding only replicate structure and sample structure over time

$$p(\mathbf{Y}) = N\big(\mathbf{Y}|\mathbf{0}, \mathbf{X}\mathbf{X}^\top + \mathbf{X}_R\mathbf{X}_R^\top + \mathbf{X}_S\mathbf{X}_S^\top \circ \mathbf{K}(\mathbf{t}, \mathbf{t}')\big) \tag{7}$$

sam Learn confounders excluding only samle structure and sample structure over time

$$p(\mathbf{Y}) = N\big(\mathbf{Y}|\mathbf{0}, \mathbf{X}\mathbf{X}^\top + \mathbf{X}_S\mathbf{X}_S^\top + \mathbf{X}_S\mathbf{X}_S^\top \circ \mathbf{K}(\mathbf{t}, \mathbf{t}')\big) \tag{8}$$

5 Results

5.1 Different Learning models

all