
Algorithm S1 NeRDS Workflow

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1: Stage 1 - Normalize and Smooth the Data
2: for components  $i = 1 : d$  do
3:   input time-course data  $(Y_i^r(t_k))_{k=1,r=1}^{n,R}$ 
4:   compute  $M_i = \max_{k,r} (Y_i^r(t_k))_{k=1,r=1}^{n,R}$ 
5:   compute  $(\tilde{Y}_i^r(t_k))_{k=1,r=1}^{n,R} = (Y_i^r(t_k)/M_i)_{k=1,r=1}^{n,R}$ 
6:   for experiments  $r = 1 : R$  do
7:     input normalized time-course data  $(\tilde{Y}_i^r(t_k))_{k=1}^n$ 
8:     compute the trajectory  $\hat{x}_i^r(t)$  using smoothing splines
9:     compute derivative  $\hat{x}_i^r(t) = \frac{d}{dt}\hat{x}_i^r(t)$ 
10:   end for
11: end for
12:
13: Stage 2 - Fit an Additive ODE
14: for components  $i = 1 : d$  do
15:   input the derivatives  $(\hat{x}_i^r(t))_{r=1}^R$  as response
16:   input the trajectories  $\{(\hat{x}_j^r(t))_{r=1}^R, j = 1, \dots, d\}$  as features
17:   input parameters  $\Lambda_1$  (smoothing) and  $\Lambda_2$  (sparsity) to search
18:
19:   Select Tuning Parameters
20:   for  $\lambda = (\lambda_1, \lambda_2) \in \Lambda_1 \times \Lambda_2$  do
21:     compute  $\hat{f}_{i+}(\lambda)$  using Sparse Backfitting [ALGORITHM S2]
22:     compute  $GCV(\lambda)$  [equation (11)]
23:   end for
24:   set  $\lambda_i \leftarrow \arg \min_{\lambda \in \Lambda_1 \times \Lambda_2} GCV(\lambda)$ 
25:
26:   output  $\hat{f}_{i+}(\lambda_i) = \sum_{j=1}^d \hat{f}_{ij}(x; \lambda_i)$ 
27: end for
28:
29: Stage 3 - Compute Coupling
30: for  $i=1:d$  do
31:   for  $j=1:d$  do
32:     input  $\hat{f}_{ij}$ 
33:     input  $\mathcal{R}_j = \text{range}(\hat{x}_j)$ 
34:     compute coupling  $\hat{\rho}_{ij}(\hat{f}_{ij}) = \int_{\mathcal{R}_j} [\hat{f}_{ij}(x)]^2 dx / |\mathcal{R}_j|$  [equation (16)]
35:   end for
36: end for
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