Appendix 2: NCA Algorithm

Given a matrix E (N x M) and a connectivity pattern Z_0, the goal is to find a decomposition of the type:

$$E = A\,\mathrm{P} \tag{B1}$$

with $A = [a_{i,j}]$ (N x L) characterized by the connectivity pattern defined by Z_0, and $P = [p_{i,j}]$ being a matrix of size (L x M). We further assume that A and P satisfy the hypotheses of Theorem 1 (Appendix 1), so that this decomposition is unique up to diagonal scaling. The optimal A and P can be found by solving:

$$\begin{aligned} &\min_{A,P} \| E - AP \|^2 \\ &\text{s.t. } A \in \mathcal{A}(Z_0) \\ &\quad a_{i,j}^{(l)} \le a_{i,j} \le a_{i,j}^{(u)} \\ &\quad p_{i,j}^{(l)} \le p_{i,j} \le p_{i,j}^{(u)} \end{aligned} \tag{B2}$$

where the norm is the matrix Frobenius norm. The box constraints defined by $a_{i,j}^{(l)}$, $a_{i,j}^{(u)}$, $p_{i,j}^{(l)}$, and $p_{i,j}^{(u)}$ are included to ensure that the elements of A and P will remain within the domain of biologically sensible values. **B2** defines a biconvex optimization problem over the manifold of matrices with connectivity pattern Z_0, i.e. given either the matrix A or the matrix P, there is always a unique least-squares solution, which allows the identification of the other matrix, and satisfies all the constraints.

This result permits us to solve the problem by using an iterative optimization algorithm, where the matrices A and P are updated in two different stages. The main steps of the algorithm are as follows:

1. **Initialization**. Initialize A_0 to be a matrix with connectivity pattern Z_0. In our implementation we set all the nonzero entries of A to an arbitrary nonzero number.

2. ***P* update**. Given A_{k-1} compute a new estimate P_k by solving the following least-squares problem:

$$\min_{P_k} \| E - A_{k-1} P_k \|^2 \quad \text{(B3)}$$
$$\text{s.t. } p_{i,j}^{(l)} \leq p_{i,j} \leq p_{i,j}^{(u)}$$

To pose the optimization problem defined by **B3** as standard least-squares estimation, we can write the matrices E and P as follows:

$$E = [e_{c,1} \quad e_{c,2} \quad \dots \quad e_{c,M}] \quad \text{(B4)}$$

$$P_k = [p_{c,1}^{(k)} \quad p_{c,2}^{(k)} \quad \dots \quad p_{c,M}^{(k)}] \quad \text{(B5)}$$

where $e_{c,i}$ is the ith column of E and $p_{c,i}^{(k)}$ is the ith column of P_k. Now define the following column vectors [size (NM x 1) and (LM x 1), respectively], which are obtained stacking the columns of E and P, respectively:

$$\mathbf{e_c} = \begin{bmatrix} e_{c,1} \\ e_{c,2} \\ \vdots \\ e_{c,M} \end{bmatrix} \qquad \mathbf{p_c^{(k)}} = \begin{bmatrix} p_{c,1}^{(k)} \\ p_{c,2}^{(k)} \\ \vdots \\ p_{c,M}^{(k)} \end{bmatrix} \quad \text{(B6)}$$

Define also the following (NM x LM) block diagonal matrix:

$$\mathbf{A_{k-1}} = \begin{bmatrix} A_{k-1} & & \cdots & 0 \\ \vdots & A_{k-1} & & \\ & & \ddots & \vdots \\ 0 & & \cdots & A_{k-1} \end{bmatrix} \quad \text{(B7)}$$

Hence, the optimization problem defined by **B3** can be written in canonical form, as follows:

$$\min_{\mathbf{p_c^{(k)}}} \| \mathbf{e_c} - \mathbf{A_{k-1}} \mathbf{p_c^{(k)}} \|^2 \quad \text{(B8)}$$
$$\text{s.t. } p_{i,j}^{(l)} \leq p_{i,j} \leq p_{i,j}^{(u)}$$

This sparse constrained least-squares problem can be solved by using a standard convex optimization technique. In our implementation, we used the SBLS algorithm developed by Björck*, which is based on the interior point method (1).

3. ***A* update**. Given P_k compute a new estimate A_k by solving the following least-squares problem:

$$\begin{aligned} &\min_{A_k} \| E - A_k P_k \|^2 \\ &\text{s.t. } A_k \in \mathcal{A}(Z_0) \\ &\quad a_{i,j}^{(l)} \le a_{i,j} \le a_{i,j}^{(u)} \end{aligned} \tag{B9}$$

The optimal A_k, satisfying the connectivity pattern constraints, can be obtained by observing that, given P_k, this problem can be decomposed, in a set of N decoupled estimation problems, where L is equal to the number of columns of A. If we write:

$$E = \begin{bmatrix} e_{r,1} \\ e_{r,2} \\ \vdots \\ e_{r,N} \end{bmatrix} \qquad A_k = \begin{bmatrix} a_{r,1}^{(k)} \\ a_{r,2}^{(k)} \\ \vdots \\ a_{r,N}^{(k)} \end{bmatrix}, \tag{B10}$$

where $e_{r,i}$ is the ith row of E and $a_{r,i}^{(k)}$ is the ith row of A_k, then **B9** is equivalent to the following set of least-squares problems:

$$\begin{aligned} &\min_{a_{r,i}^{(k)}} \| e_{r,i} - a_{r,i}^{(k)} P_k \|^2 \qquad i = 1, \ldots, N \\ &\text{s.t. } A_k \in \mathcal{A}(Z_0) \\ &\quad a_{i,j}^{(l)} \le a_{i,j} \le a_{i,j}^{(u)} \end{aligned} \tag{B11}$$

The connectivity constraints on A_k can be removed simply by eliminating from each $a_{r,i}^{(k)}$ those elements that are constrained to be identically zero, resulting in a new set of row vectors $\tilde{a}_{r,i}^{(k)}$. Thus **B11** becomes:

$$\begin{aligned} &\min_{\tilde{a}_{r,i}^{(k)}} \| e_{r,i} - \tilde{a}_{r,i}^{(k)} \tilde{P}_k \|^2 \qquad i = 1, \ldots, N \\ &\text{s.t. } a_{i,j}^{(l)} \le a_{i,j} \le a_{i,j}^{(u)} \end{aligned} \tag{B12}$$

where $\widetilde{P}_k$ is obtained from P_k by removing the rows corresponding to the identically zero entries of $a_{r,i}$. This set of constrained least-squares problems can be solved by using the same optimization procedure used to solve **B8**.

4. **Convergence criterion.** If the decrease in total least-square error, at the end of step 3, is above a predetermined value, repeat from step 2. The convergence threshold can be selected according to the desired degree of accuracy.

Because in each step of the iterative optimization procedure, the estimation error is guaranteed to be nonincreasing, convergence to the optimal solution is assured as long as the hypotheses of Theorem 1 are satisfied.

Reference:

1. Mehrotra, S. (1992) *SIAM J. Optimization* **2**, 575-601.

Footnote:

* Bjorck, A. & Lundquist, M., the Second SIAM Conference on Sparse Matrices, Oct. 9-11, 1996, Coeur d'Alene, ID.