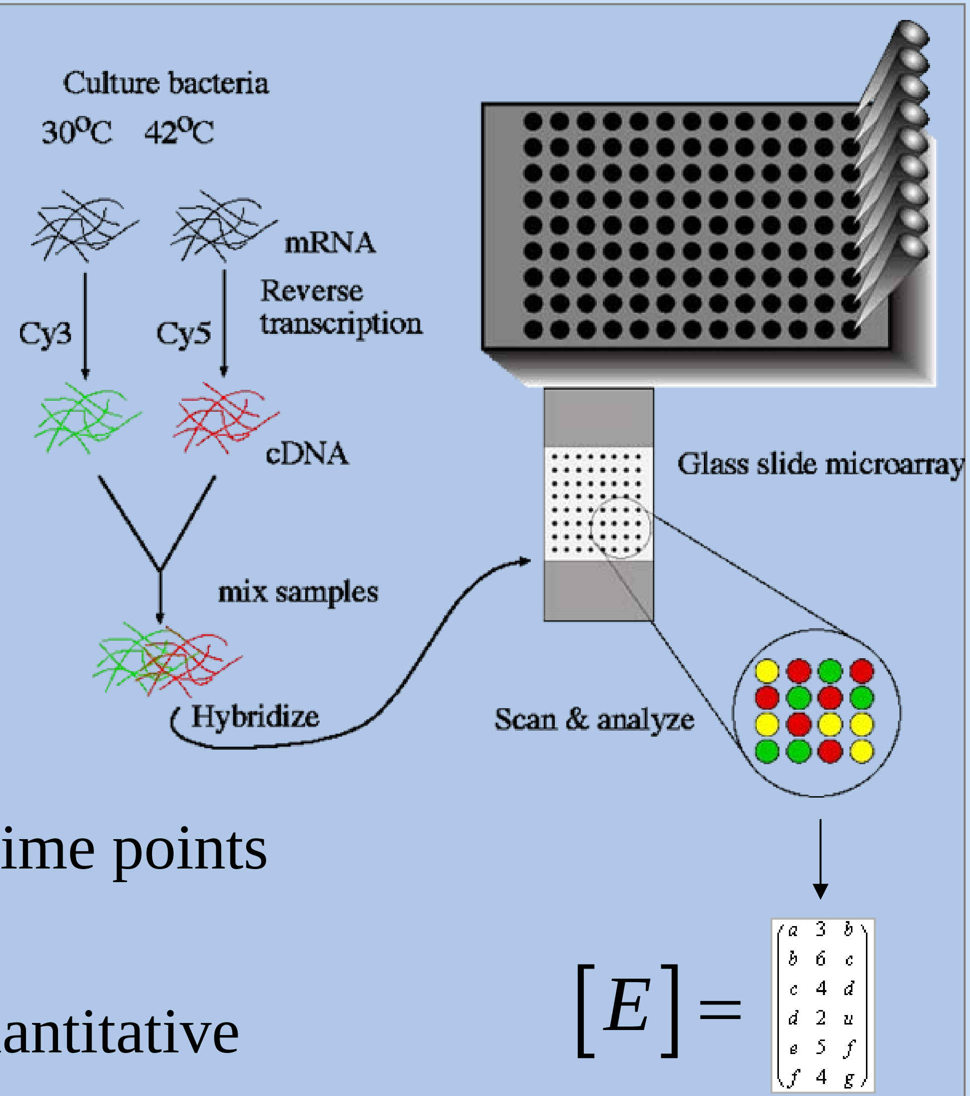
Large Networks:
Network Component Analysis (NCA)

blablablatt

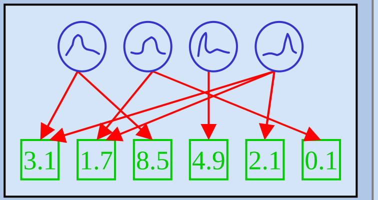
Data for NCA

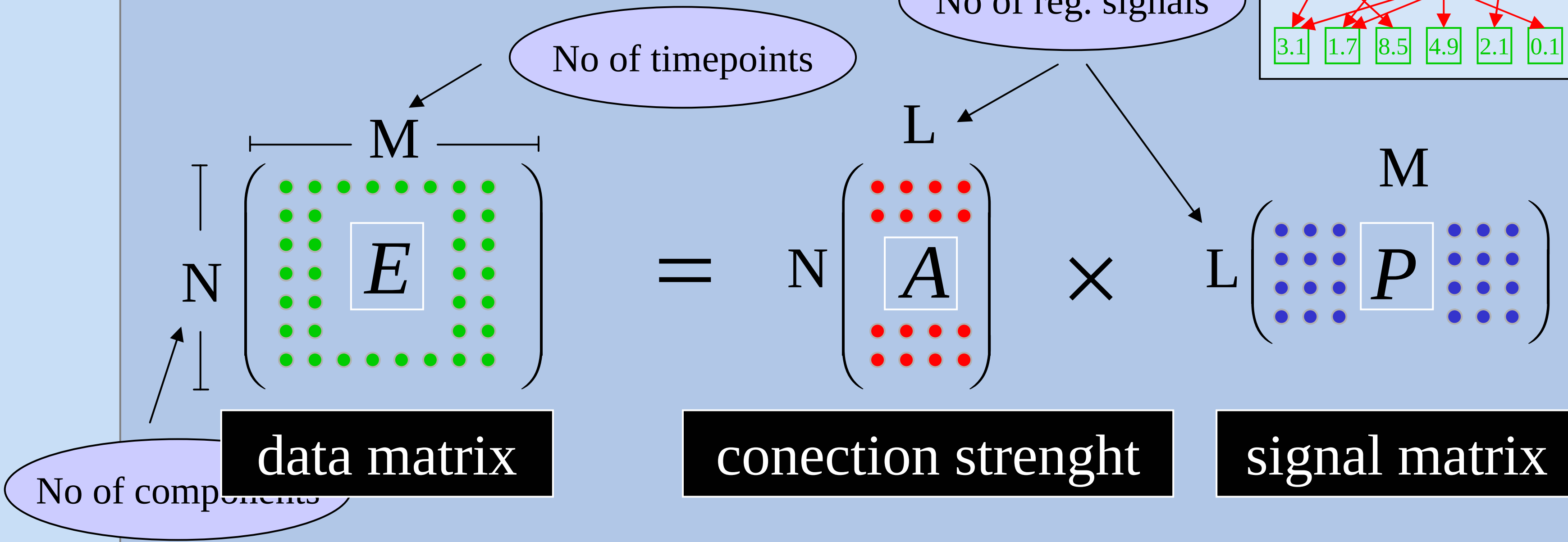


Microarray

- take samples over time points
- extract mRNA
- measure mRNA quantitative

Basic concept





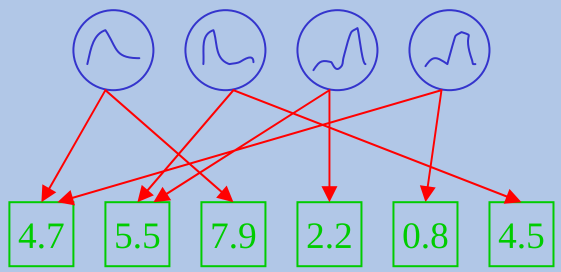
Is this decomposition unique?

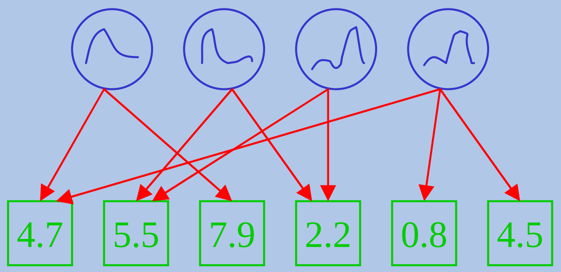
$$[E] = ([A][X])([X^{-1}][P]) = [\bar{A}][\bar{P}]$$

→ Proof by Liao et al. 2003 showed that x_{ij} is only a scaling factor

Criteria for the NCA

i) The connectivity matrix [A] must have full-colum rank.



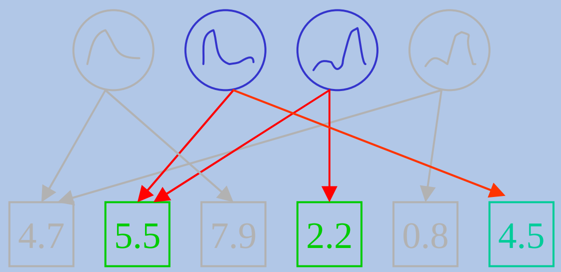


$$A_1 = \begin{pmatrix} 5 & 0 & 0 & 2 \\ 0 & 2 & 4 & 0 \\ 3 & 0 & 0 & 0 \\ 0 & 0 & 5 & 0 \\ 0 & 0 & 0 & 6 \\ 0 & 8 & 0 & 0 \end{pmatrix}$$

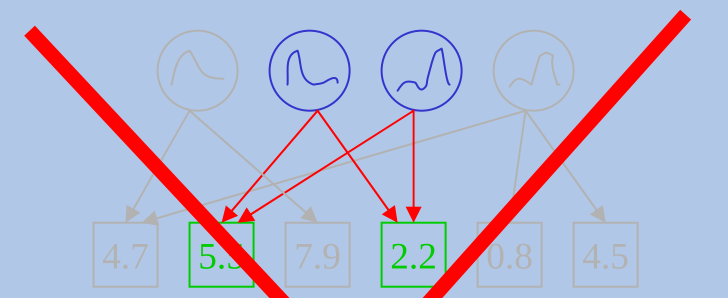
$$A_2 = \begin{pmatrix} 5 & 0 & 0 & 2 \\ 0 & 2 & 4 & 0 \\ 3 & 0 & 0 & 0 \\ 0 & 3 & 6 & 0 \\ 0 & 0 & 0 & 6 \\ 0 & 0 & 0 & 8 \end{pmatrix}$$

Criteria for the NCA

i) The connectivity matrix [A] must have full-colum rank.



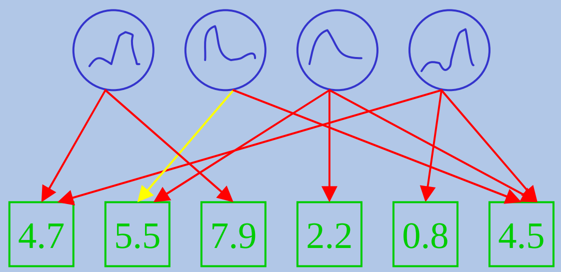
$$A_1 = \begin{pmatrix} 5 & 0 & 0 & 2 \\ 0 & 2 & 4 & 0 \\ 3 & 0 & 0 & 0 \\ 0 & 0 & 5 & 0 \\ 0 & 0 & 0 & 6 \\ 0 & 8 & 0 & 0 \end{pmatrix}$$

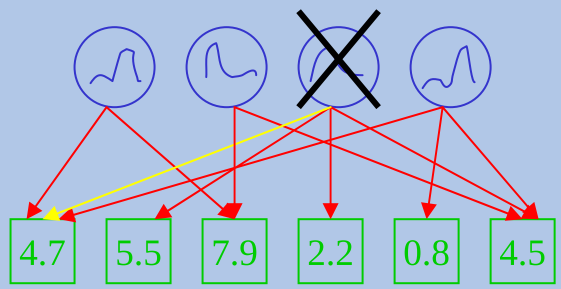


$$A_2 = \begin{pmatrix} 5 & 0 & 0 & 2 \\ 0 & 2 & 4 & 0 \\ 3 & 0 & 0 & 0 \\ 0 & 3 & 6 & 0 \\ 0 & 0 & 0 & 6 \\ 0 & 0 & 0 & 8 \end{pmatrix}$$

Criteria for the NCA

ii) Sub-matrixes [A_{r_i}] must have full-colum rank.



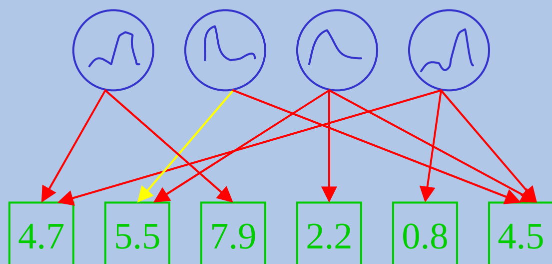


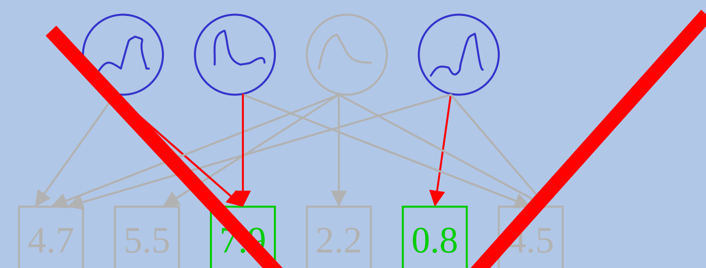
$$A_1 = \begin{pmatrix} 2 & 0 & 0 & 1 \\ 0 & 5 & 4 & 0 \\ 8 & 1 & 0 & 0 \\ 0 & 0 & 6 & 0 \\ 0 & 0 & 0 & 7 \\ 0 & 3 & 5 & 1 \end{pmatrix}$$

$$Ar_2 = \begin{pmatrix} 5 & 0 & 2 & 1 \\ 0 & 0 & 4 & 0 \\ 2 & 1 & 0 & 0 \\ 0 & 0 & 3 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & 4 & 8 & 9 \end{pmatrix}$$

Criteria for the NCA

ii) Sub-matrixes [A_{r_i}] must have full-colum rank.





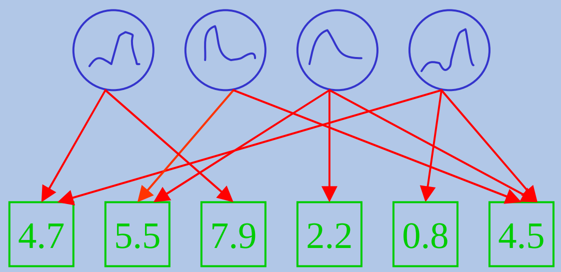
No unique solution

$$A_1 = \begin{pmatrix} 2 & 0 & 0 & 1 \\ 0 & 5 & 4 & 0 \\ 8 & 1 & 0 & 0 \\ 0 & 0 & 6 & 0 \\ 0 & 0 & 0 & 7 \\ 0 & 3 & 5 & 1 \end{pmatrix}$$

$$Ar_2 = \begin{pmatrix} 5 & 0 & 2 & 1 \\ 0 & 0 & 4 & 0 \\ 2 & 1 & 0 & 0 \\ 0 & 0 & 3 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & 4 & 8 & 9 \end{pmatrix} = \begin{pmatrix} 2 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix}$$

Criteria for the NCA

iii) The signal matrix [P] must have full-row rank.



$$P = L \overbrace{\begin{pmatrix} 1 & 3 & 4 & 7 & 3 & 1 \\ 3 & 8 & 4 & 2 & 3 & 1 \\ 2 & 7 & 5 & 4 & 1 & 2 \\ 1 & 2 & 1 & 5 & 8 & 3 \end{pmatrix}}^{M}$$

⟶ Can not be tested *a priori*!

⟶ Implies that we need more time points [M] than regulatory units [L]

Method for NCA

$$\min \left\| [E] - [A][P] \right\|^2 \qquad s.t. A \in Z_0$$

$$\min \left\| \begin{pmatrix} 3.5 & 4.0 & 1.2 & 4.7 & 0.2 & 0.1 & 0.1 & 0.1 \\ 0.5 & 1.2 & 4.5 & 6.7 & 8.0 & 4.7 & 3.2 & 1.5 \\ 4.7 & 6.7 & 3.2 & 4.7 & 4.0 & 1.2 & 4.7 & 0.1 \\ 8.0 & 3.2 & 4.7 & 4.0 & 6.7 & 3.2 & 8.0 & 0.1 \\ 4.0 & 3.2 & 8.0 & 4.7 & 4.7 & 0.1 & 3.2 & 0.2 \\ 3.2 & 6.7 & 1.2 & 8.0 & 4.7 & 8.0 & 4.7 & 1.2 \end{pmatrix} - \begin{pmatrix} rnd & 0 & 0 & rnd \\ 0 & rnd & rnd & 0 \\ rnd & rnd & 0 & 0 \\ 0 & 0 & rnd & 0 \\ 0 & 0 & 0 & rnd \\ 0 & rnd & rnd & rnd \end{pmatrix} \begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \right\|^2$$

↓

Solver → unique [A][P]

Transfer into log space

E: expression level
c: connection strength
T: regulatory signal

$$E_i(t)=\sum_{j=1}^{L} c_j T_j = c_1T_1 + c_2T_2 + \ldots c_L T_L$$

$$\frac{E_i(t)}{E_i(0)}=\prod_{j=1}^{L}\left(\frac{T_j(t)}{T_j(0)}\right)^{c_{ij}}=\left(\frac{T_1(t)}{T_1(0)}\right)^{c_{i1}} * \ldots * \left(\frac{T_L(t)}{T_L(0)}\right)^{c_{iL}}$$

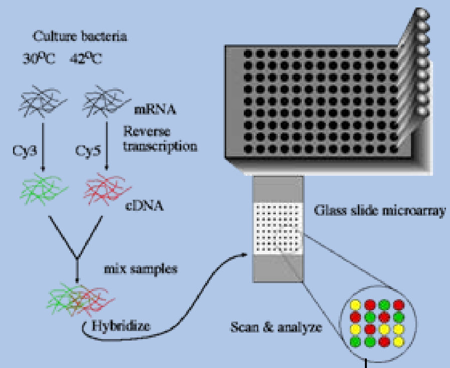
$$\longrightarrow \quad \log[Er]=[C]\log[Tr]$$

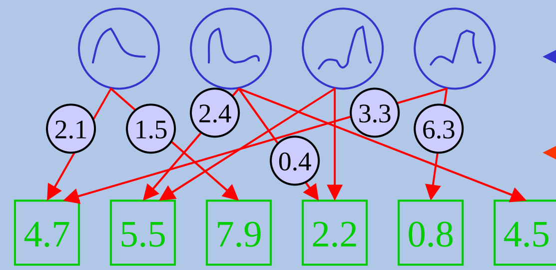
$$Er_{ij}=\frac{E_{ij}(t)}{E_{ij}(0)} \qquad Tr_{ij}=\frac{T_{ij}(t)}{T_{ij}(0)}$$

Advantages:

- computational traceable
- approximate quadratic model
- relative values

NCA step-by-step





$$[E] = \begin{pmatrix} 3.5 & 4.0 & 1.2 & 4.7 & 0.2 & 0.1 & 0.1 & 0.1 \\ 0.5 & 1.2 & 4.5 & 6.7 & 8.0 & 4.7 & 3.2 & 1.5 \\ 4.7 & 6.7 & 3.2 & 4.7 & 4.0 & 1.2 & 4.7 & 0.1 \\ 8.0 & 3.2 & 4.7 & 4.0 & 6.7 & 3.2 & 8.0 & 0.1 \\ 4.0 & 3.2 & 8.0 & 4.7 & 4.7 & 0.1 & 3.2 & 0.2 \\ 3.2 & 6.7 & 1.2 & 8.0 & 4.7 & 8.0 & 4.7 & 1.2 \end{pmatrix}$$

$$[A] = \begin{pmatrix} rnd & 0 & 0 & rnd \\ 0 & rnd & rnd & 0 \\ rnd & rnd & 0 & 0 \\ 0 & 0 & rnd & 0 \\ 0 & 0 & 0 & rnd \\ 0 & rnd & rnd & rnd \end{pmatrix}$$

$$[P] = \begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

$$\min \left\| [E] - [A][P] \right\|^2 \quad s.t. A \in Z_0$$